NORTH CAROLINA Medical Journal

Vol. 21 No. 2
February, 1960

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ROENTGENOLOGIC CHANGES IN SALMONELLA OSTEOMYELITIS

— WILLIAM A. DUNNAGAN, M.D. —

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Official Organ of

THE MEDICAL SOCIETY OF THE STATE OF NORTH CAROLINA

VOLUME 21
NUMBER 2

FEBRUARY, 1960

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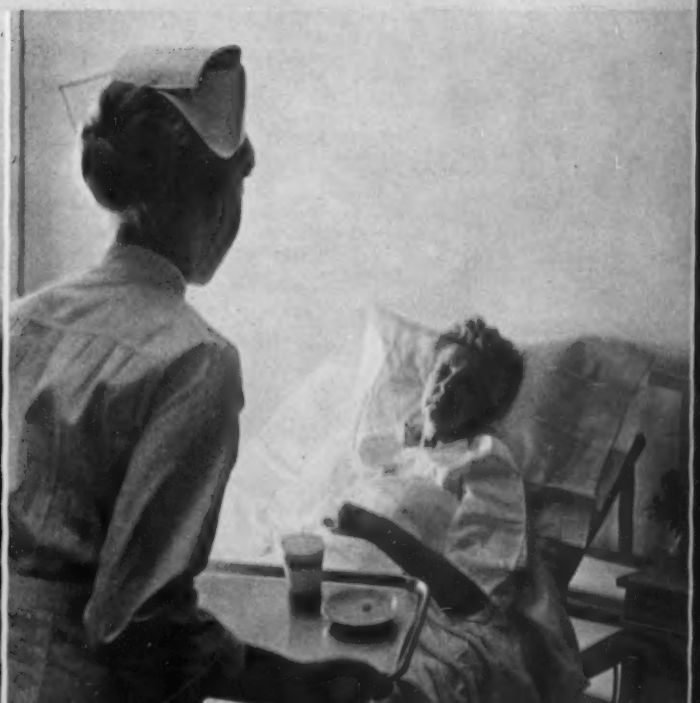

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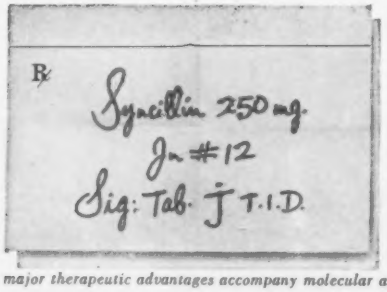
Significance of higher blood levels with SYNCILLIN

Higher blood levels may be of value with organisms of only moderate penicillin sensitivity where doubling the blood concentration may be essential for effective bactericidal action. In addition, these higher levels may be necessary where there is infection in areas with a poor blood supply.[6] Under these circumstances a higher blood concentration may provide the increased diffusion pressure required to deliver adequate amounts to the tissue. Also, antibiotic activity of SYNCILLIN is directly proportional to oral dosage. Increasing the dosage may, therefore, enhance the drug's effectiveness in certain cases.

Efficacy of SYNCILLIN against staphylococci and other resistant organisms

Studies have shown that SYNCILLIN is effective *in vitro* against 60 to 75% of hospital "staph" strains, while penicillin G and penicillin V are now effective against only 30 to 50%.[1, 2] Therefore, if clinical judgment indicates the use of penicillin, SYNCILLIN would be expected to be the most effective. However, since some strains are still resistant to SYNCILLIN as well as to the other penicillins, cultures and sensitivity tests should be performed where indicated by clinical judgment.

There have recently been reports of decreased efficacy of penicillin in streptococcal[3] and gonococcal[4, 5] infections. The emergence of penicillin-resistant gonococci appears to be associated with an increase in the incidence of gonorrhea all over the world. When a less sensitive strain is encountered the higher blood levels produced by SYNCILLIN may be most helpful.



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Relation of intermittent high blood levels of SYNCILLIN to antibacterial efficacy

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Reduced rate of inactivation of SYNCILLIN by staph penicillinase

Bacterial resistance to penicillin has been attributed to the action of penicillin-inactivating enzymes produced by the invading organisms. **SYNCILLIN** is less affected by staphylococcal penicillinase than either of its component isomers. Further, **SYNCILLIN** is shown to be less inactivated by this enzyme than penicillin V and penicillin G. Penicillinase from *B. cereus* likewise inactivates **SYNCILLIN** less rapidly than penicillin V and G. But this would not impede the therapeutic use of this penicillinase in allergic reactions. This is because the massive dosage with which this enzyme is administered would effectively destroy **SYNCILLIN** in the body.

References: 1. Wright, W. W.: Microbiology Report to Bristol Laboratories Inc. 2. Kligman, A.; Morigi, E. M. E.; Wheatley, W. B., and Albright, H.: Paper presented at the Seventh Antibiotic Symposium, November 4-6, Washington, D.C. 3. Editorial: New England J. Med. **261**:305 (Aug. 6) 1959. 4. King, A.: Lancet **1**:651 (March 29) 1958. 5. Epstein, E.: J.A.M.A. **169**:1055 (March 7) 1959. 6. Kass, E. H.: Am. J. Med. **18**:764 (May) 1955. 7. Eagle, H.: J. Bact. **58**:475, 1949.

Indications: **SYNCILLIN** is recommended in the treatment of infections caused by pneumococci, streptococci, gonococci, corynebacteria, and penicillin-sensitive staphylococci. In addition, **SYNCILLIN** is effective against certain strains of staphylococci resistant to other penicillins. **SYNCILLIN**, like other oral penicillins, is not recommended at the present time in deep-seated or chronic infections, subacute bacterial endocarditis, meningitis, or syphilis.

Dosage: 125 mg. or 250 mg. three times daily, depending on the severity of infection. Larger doses (e.g., 500 mg. t.i.d.) may be used for more severe infections. **SYNCILLIN** may be administered without regard to meals. Beta hemolytic streptococcal infections should be treated with **SYNCILLIN** for at least ten days.

Precautions: At the present time it is not possible to draw definite conclusions regarding the incidence of allergenicity to **SYNCILLIN** or its cross-allergenicity with natural penicillins. *Therefore, the usual precautions for oral penicillin therapy should always be observed.* Patients with histories of asthma, hay fever, urticaria, or previous reactions to penicillin should be watched with special care. Administration of oral penicillin, in rare instances, may provoke acute anaphylaxis, particularly in penicillin-sensitive individuals.
Diarrhea has been reported occasionally following heavy dosage. If this occurs, lengthen the interval between dosages.
If superinfection occurs during therapy, appropriate measures should be taken. Since some strains of staphylococci are resistant to **SYNCILLIN** as well as to other penicillins, cultures and sensitivity tests should be performed where indicated by clinical judgment. As is true with all antibiotics, clinical response does not always correlate with laboratory bacterial sensitivity reports.

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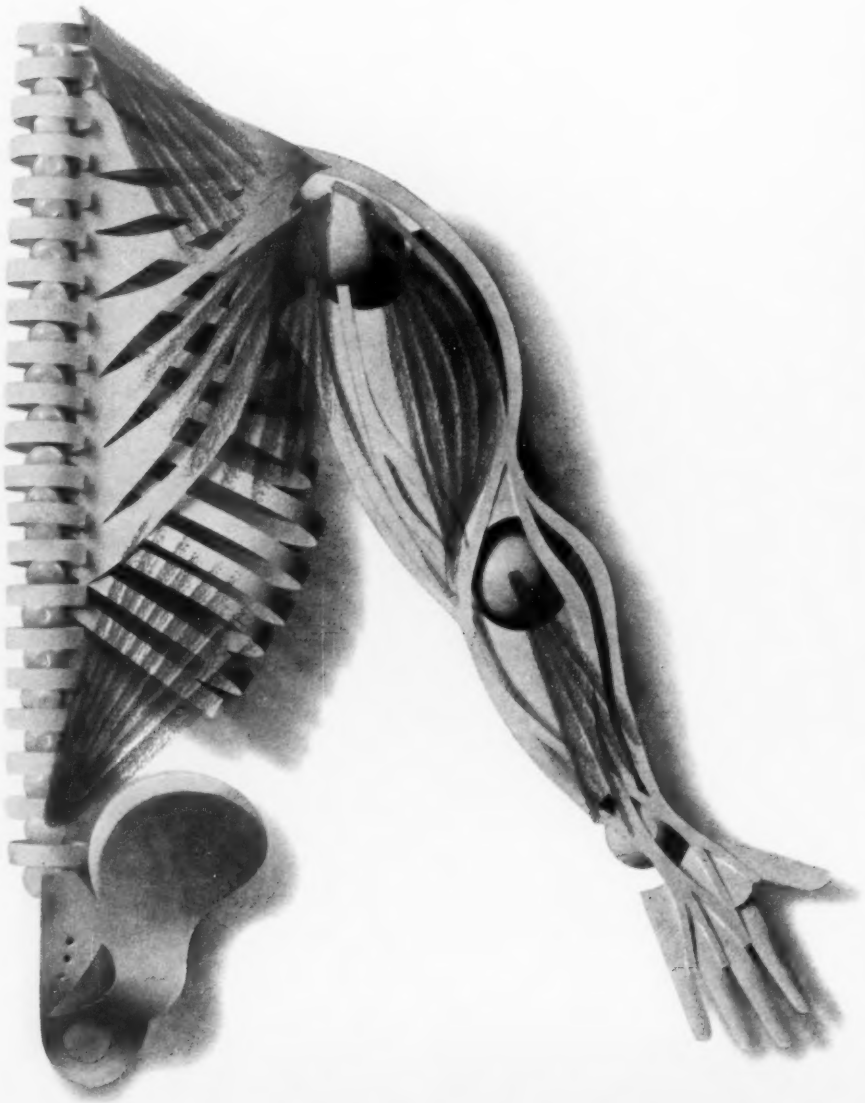

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Wein, A. B.: The Use of Carisoprodol in Orthopedic Surgery and Rehabilitation. Proceedings of the Symposium on The Pharmacology and Clinical Usefulness of Carisoprodol. Wayne State University Press, Detroit, 1959, p. 156.

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Cooper, C. D., and Epstein, J. H.: The Clinical Evaluation of Carisoprodol by a double-blind technique. Ibid. p. 97.

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1. Kuge, T.: To be published. H-227

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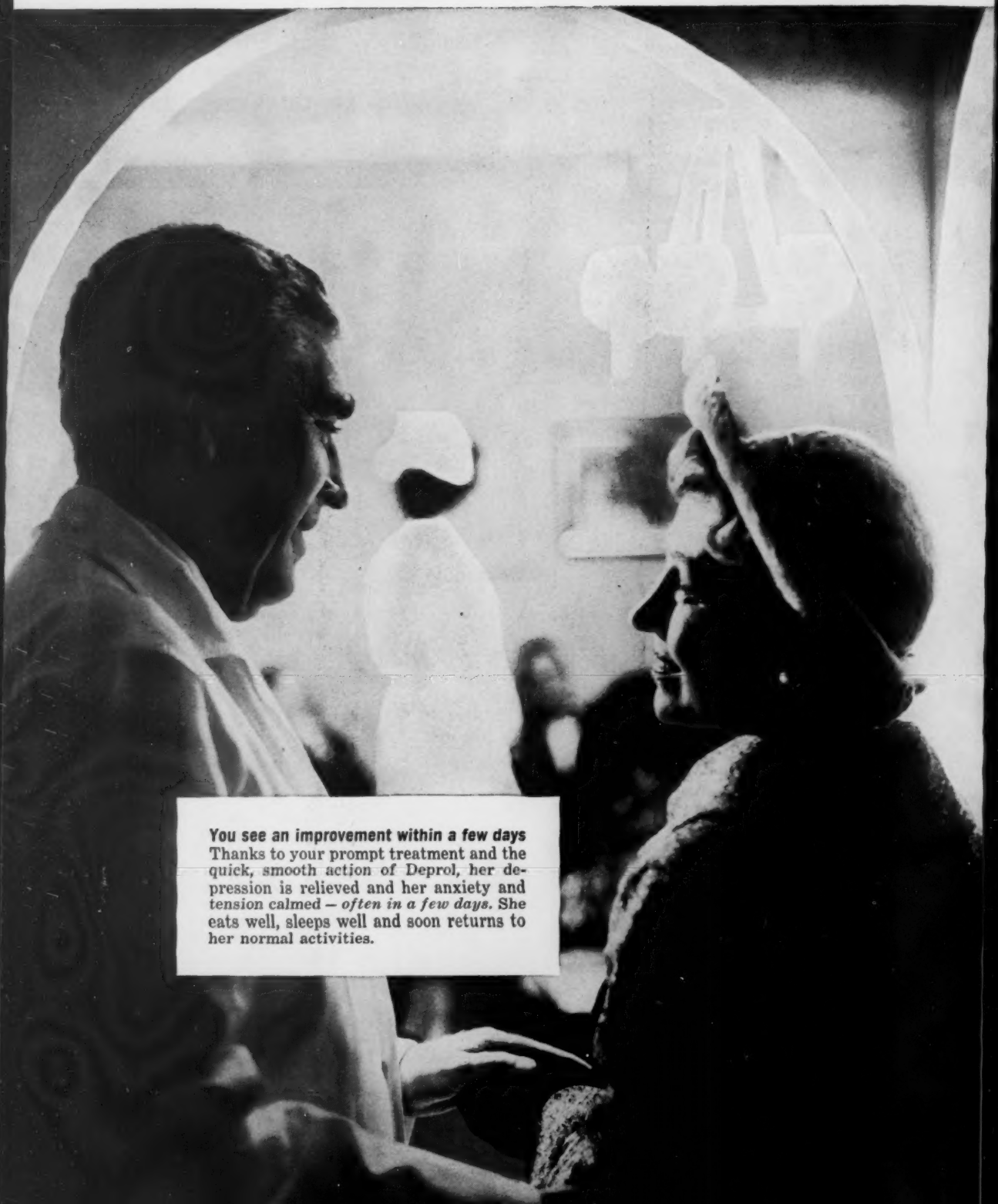

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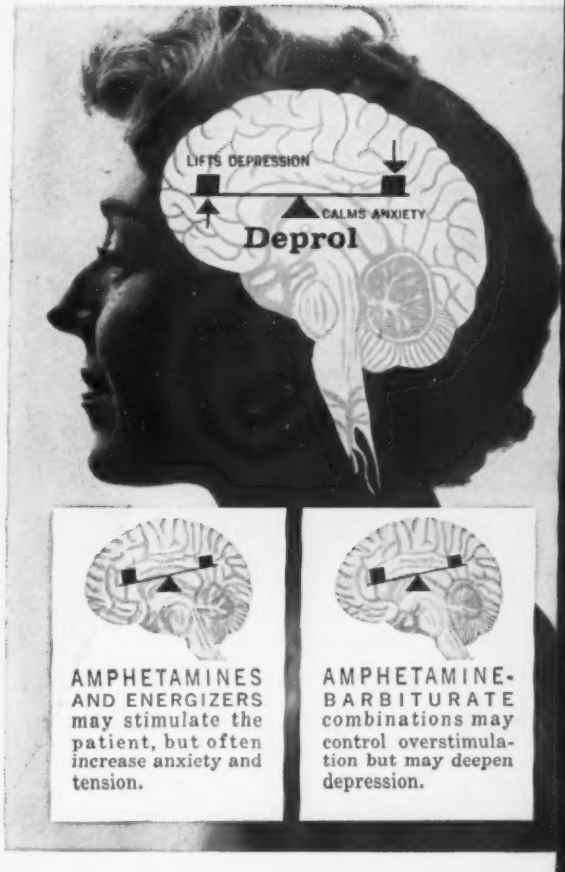
Acts swiftly – the patient often feels better within a few days. Unlike the delayed action of other drugs which may take two to six weeks to bring results, Deprol's smooth, immediate action relieves the patient quickly – often within a few days.

Acts safely – no danger of liver damage. Deprol does not produce liver damage, hypotension, psychotic reactions or changes in sexual function – frequently reported with other drugs.


LIFTS DEPRESSION
CALMS ANXIETY
Deprol
AMPHETAMINES AND ENERGIZERS may stimulate the patient, but often increase anxiety and tension.
AMPHETAMINE-BARBITURATE combinations may control overstimulation but may deepen depression.

BIBLIOGRAPHY *(10 clinical studies, 714 patients)*:

1. Alexander, L. (35 patients): Chemotherapy of depression – Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. *J.A.M.A. 166:1019, March 1, 1958.* **2.** Bateman, J. C. and Carlton, H. M. (50 patients): Meprobamate and benactyzine hydrochloride (Deprol) as adjunctive therapy for patients with advanced cancer. Antibiotic Med. & Clin. Therapy 6:648, Nov. 1959. **3.** Bell, J. L., Tauber, H., Santy, A. and Pulito, F. (77 patients): Treatment of depressive states in office practice. Dis. Nerv. System 20:263, June 1959. **4.** Breitner, C. (31 patients): On mental depressions. Dis. Nerv. System 20:142, (Section Two), May 1959. **5.** McClure, C. W., Papas, P. N., Speare, G. S., Palmer, E., Slattery, J. J., Konefal, S. H., Henken, B. S., Wood, C. A. and Ceresia, G. B. (128 patients): Treatment of depression–New technics and therapy. Am. Pract. & Digest Treat. 10:1525, Sept. 1959. **6.** Pennington, V. M. (135 patients): Meprobamate-benactyzine (Deprol) in the treatment of chronic brain syndrome, schizophrenia and senility. J. Am. Geriatrics Soc. 7:656, Aug. 1959. **7.** Rickels, K. and Ewing, J. H. (35 patients): Deprol in depressive conditions. Dis. Nerv. System 20:364, (Section One), Aug. 1959. **8.** Ruchwarger, A. (87 patients): Use of Deprol (meprobamate combined with benactyzine hydrochloride) in the office treatment of depression. M. Ann. District of Columbia 28:438, Aug. 1959. **9.** Settel, E. (52 patients): Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Antibiotic Med. & Clin. Therapy. In press, 1959. **10.** Splitter, S. R. (84 patients): The care of the anxious and the depressed. Submitted for publication, 1959.

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be gradually increased up to 3 tablets q.i.d.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

▲Deprol▲®

WALLACE LABORATORIES / *New Brunswick, N. J.*

This is Panalba performance...

in sinusitis

. . . into a mixed culture of the four organisms commonly involved in sinusitis . . . *Str. hemolyticus, D. pneumoniae, H. influenzae* and *Staph. aureus* (in this case a resistant strain) . . . we introduce the five most frequently used antibiotics.

Twenty-four hours later (in this greatly enlarged photograph), note that only *one* of the five leading antibiotics has stopped *all* the organisms, including the resistant staph! This is Panalba.

In your next patient with sinusitis . . . in *all* your patients with potentially-serious infections . . . provide this extra protection with your prescription:

Dosage—1 or 2 capsules 3 or 4 times a day.
Supplied—Capsules containing Panmycin phosphate equivalent to 250 mg. tetracycline hydrochloride, and 125 mg. Albamycin as novobiocin sodium, in bottles of 16 and 100.
Now available: **new Panalba Half-Strength Capsules in bottles of 16 and 100.**

Panalba*

(Panmycin® Phosphate plus Albamycin®)

The broad-spectrum antibiotic of *first* resort

Upjohn The Upjohn Company
Kalamazoo, Michigan

*TRADEMARK, REG. U. S. PAT. OFF.

Donnagel®

Robins

or Donnagel® with Neomycin

Prompt and more dependable control of virtually all diarrheas can be achieved with the comprehensive DONNAGEL formula, which provides adsorbent, demulcent, antispasmodic and sedative effects—with or without an antibiotic. Early re-establishment of normal bowel function is assured—for all ages, in all seasons.

DONNAGEL: In each 30 cc. (1 fl. oz.):

Kaolin (90 gr.)	6.0 Gm.
Pectin (2 gr.)	142.8 mg.
Hyoscyamine sulfate	0.1037 mg.
Atropine sulfate	0.0194 mg.
Hyoscine hydrobromide	0.0065 mg.
Phenobarbital (¼ gr.)	16.2 mg.

DONNAGEL WITH NEOMYCIN

Same formula, plus

Neomycin sulfate	300 mg.

(Equal to neomycin base, 210 mg.)

A. H. ROBINS CO., INC., Richmond 20, Virginia · *Ethical Pharmaceuticals of Merit since 1878*

Synonyms for Pain Relief...

'TABLOID'

'EMPIRIN' COMPOUND®

Acetophenetidin ..... gr. 2½
Acetylsalicylic Acid .... gr. 3½
Caffeine ..... gr. ½

'TABLOID'

'EMPIRIN' COMPOUND® WITH CODEINE PHOSPHATE*

No. 1
Acetophenetidin ..... gr. 2½
Acetylsalicylic Acid .... gr. 3½
Caffeine ..... gr. ½
Codeine Phosphate .... gr. ⅛

No. 2
Acetophenetidin ..... gr. 2½
Acetylsalicylic Acid .... gr. 3½
Caffeine ..... gr. ½
Codeine Phosphate .... gr. ¼

No. 3
Acetophenetidin ..... gr. 2½
Acetylsalicylic Acid .... gr. 3½
Caffeine ..... gr. ½
Codeine Phosphate .... gr. ½

No. 4
Acetophenetidin ..... gr. 2½
Acetylsalicylic Acid .... gr. 3½
Caffeine ..... gr. ½
Codeine Phosphate .... gr. 1

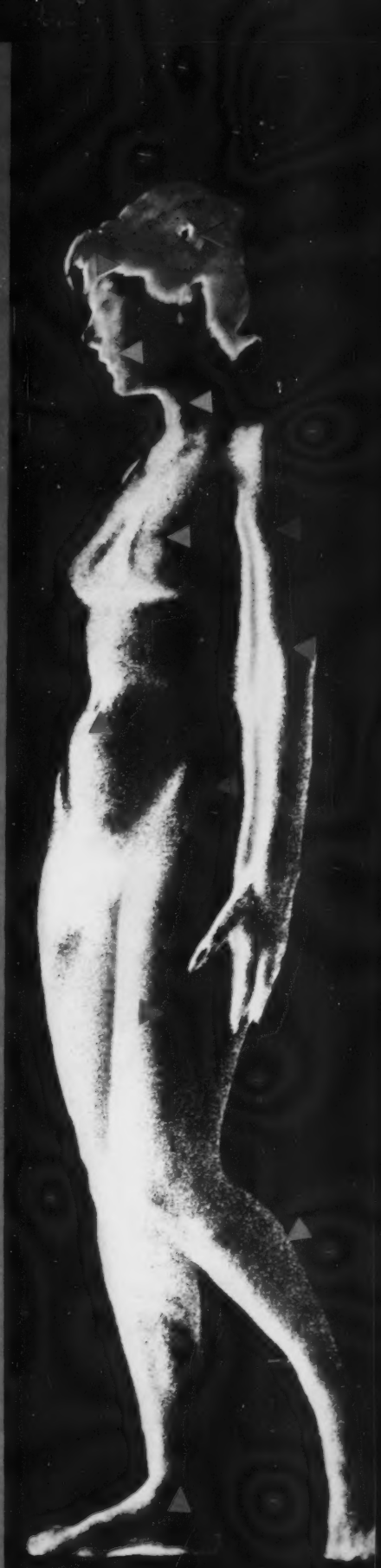
*Subject to Federal Narcotic Regulations

...providing the desired gradation of potencies for relief of varying intensities of pain

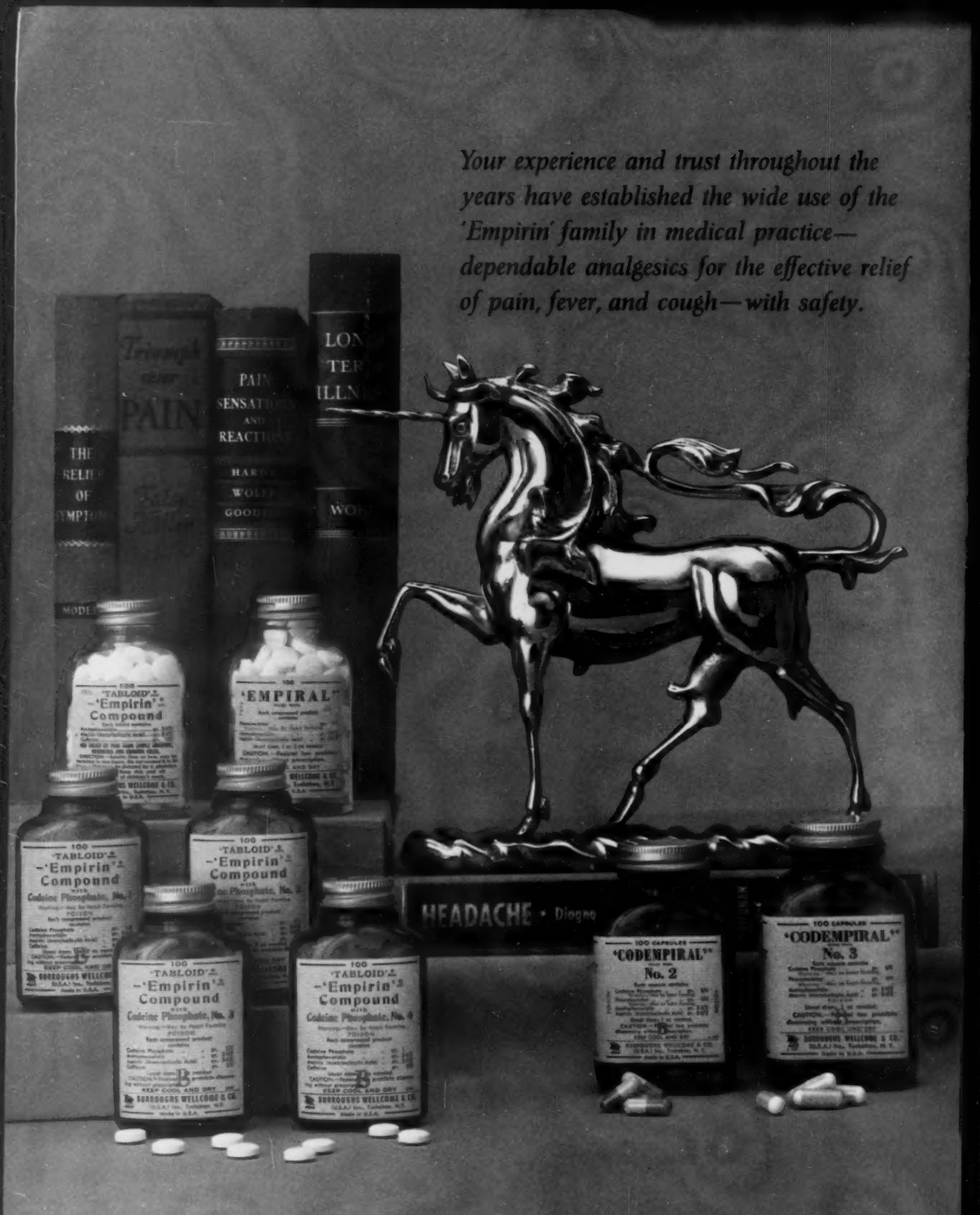
IN
simple headache
rheumatic conditions
arthralgias
myalgias
common cold
toothache
earache
dysmenorrhea
neuralgia
minor trauma
tension headache
premenstrual tension
minor surgery
post-partum pain
trauma
organic disease
neoplasm
muscle spasm
colic
migraine
musculo-skeletal pains
postdental surgery
post-partum involution
fractures
synovitis/bursitis

relief of pain
of all degrees of
severity up to
that which
requires morphine

AND IN
fevers
dry,
unproductive coughs



BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York


Your experience and trust throughout the years have established the wide use of the 'Empirin' family in medical practice—dependable analgesics for the effective relief of pain, fever, and cough—with safety.
'TABLOID' -'Empirin' Compound
'EMPIRAL'
'CODEMPIRAL' No. 2
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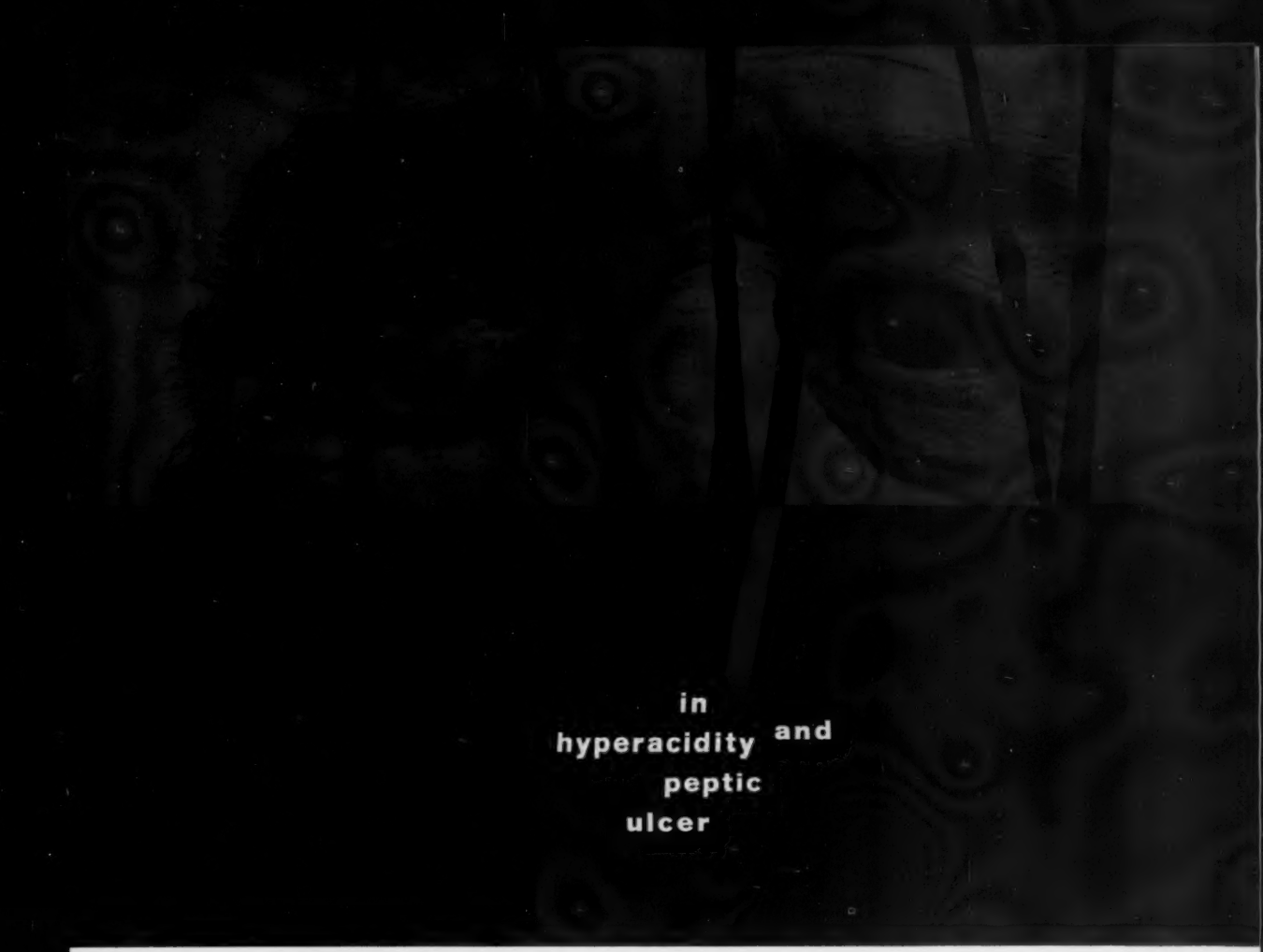
HEADACHE
BURROUGHS WELLCOME & CO. (U.S.A.) INC.
Tuckahoe, New York



as reactive in tablet form . . .

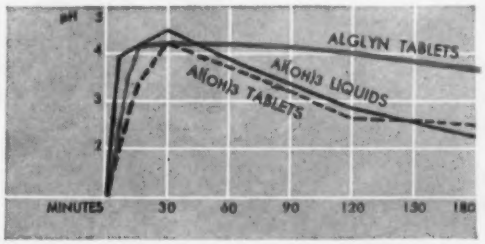
ALGLYN®

Dihydroxy aluminum aminoacetate

The superiority of Alglyn (dihydroxy aluminum aminoacetate) as an antacid over ordinary aluminum preparations is quite pronounced. Not only do Alglyn Tablets act as rapidly as aluminum hydroxide gels and magmas, but they maintain a much more effective pH for a longer time (see chart).

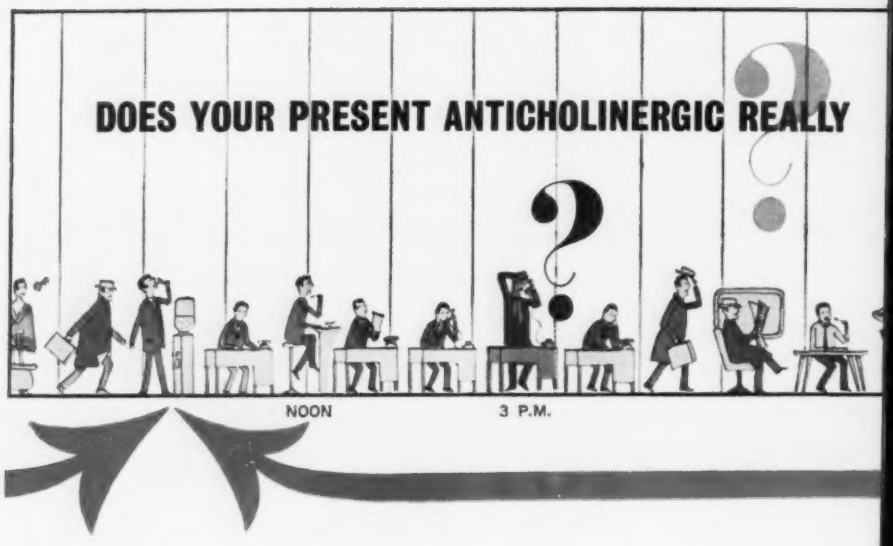
Furthermore, Alglyn Tablets are decidedly superior when antacid-belladonna therapy is indicated. Ordinary aluminum preparations may actually *ad*sorb as much as 80% of the spasmolytic drug, as compared to only 7% for Alglyn Tablets. In addition, Alglyn contains no sodium and less aluminum.

Supplied in bottles of 100 0.5 Gm. tablets. Also as Belglyn® (with belladonna), and as Malglyn® (with belladonna and phenobarbital). Literature available upon request.



BRAYTEN

BRAYTEN PHARMACEUTICAL COMPANY *Chattanooga 9, Tennessee*



The test—you might say the acid test—of an anticholinergic is simple: will it protect your patient from hyperacidity around the clock, **even while he sleeps.** The weakness of t.i.d. or q.i.d. preparations is well recognized; but even some "b.i.d." encapsulations may be unreliable. McHardy, for instance, found a "widely variable duration of action, definitely less than that anticipated" in the "sustained," "delayed," and "gradual release" anticholinergics he studied.[1]

COMPARE THE DATA ON ENARAX... the new combination of an **inherently** long-acting anticholinergic (oxyphencyclimine) and Atarax, the non-secretory tranquilizer. Note the effectiveness of oxyphencyclimine:

OBSERVE THE OXYPHENCYCLIMINE REPORTS...

McHardy: "[Oxyphencyclimine] has proved to be an excellent sustained-action anticholinergic in our study of this agent over a period of eighteen months."[1]

Kemp: "...for the majority of patients, one tablet every 12 hours provided adequate control. This characteristic long action...may constitute an advantage of this drug as compared to coated 'long-acting' preparations of other compounds."[3]

Add Atarax to this 12-hour anticholinergic. The resulting combination—ENARAX—now gives relief from emotional stress, in addition to a reduction of spasm and acid. Atarax does not stimulate gastric secretion. No serious adverse clinical reaction has ever been documented with Atarax.

LOOK AT THE RESULTS WITH ENARAX[4,5]:

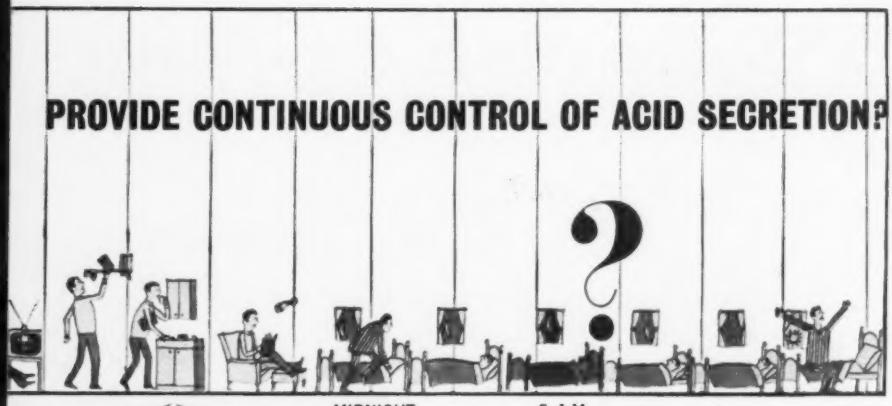
Does the medication you now prescribe assure you of all these benefits? If not, why not put your next patient with peptic ulcer or G.I. dysfunction on therapy that **does.**

ENARAX®

(oxyphencyclimine plus ATARAX®)

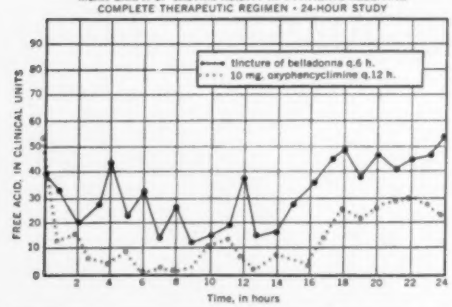
A SENTRY FOR THE G.I. TRACT

PROVIDE CONTINUOUS CONTROL OF ACID SECRETION?



"Prolonged periods of achlorhydria" after 10 mg. oxyphencyclimine q. 12 h.[1]

MEAN GRAPH OF GASTRIC ACIDITY IN 4 PATIENTS RECEIVING COMPLETE THERAPEUTIC REGIMEN • 24-HOUR STUDY



Clinical Diagnosis: Peptic Ulcer—Gastritis—Gastroenteritis—Colitis—Functional Bowel Syndrome—Duodenitis—Hiatus Hernia (symptomatic)—Irritable Bowel Syndrome—Pylorospasm—Cardiospasm—Biliary Tract Dysfunctions—and Dysmenorrhea.

Clinical Results: Effective in over 92% of cases.

As for Safety: "Side reactions were uncommon, usually no more than dryness of the mouth. . . ."[4]

Each ENARAX tablet contains:

Oxyphencyclimine HCl ..... 10 mg.
Hydroxyzine (ATARAX®) ..... 25 mg.

Dosage: One-half to one tablet twice daily—preferably in the morning and before retiring. The maintenance dose should be adjusted according to therapeutic response. Use with caution in patients with prostatic hypertrophy and with ophthalmological supervision only in glaucoma.

Supplied: In bottles of 60 black-and-white scored tablets.

References: 1. McHardy, G., et al.: J. Louisiana M. Soc. 111:290 (Aug.) 1959. 2. Steigmann, F.: Study conducted at Cook County Hospital, Chicago, Illinois, in press. 3. Kemp, J. A.: Antibiotic Med. & Clin. Therapy 6:534 (Sept.) 1959. 4. Leming, B. H., Jr.: Clin. Med. 6:423 (Mar.) 1959. 5. Data in Roerig Medical Department files.

ROERIG

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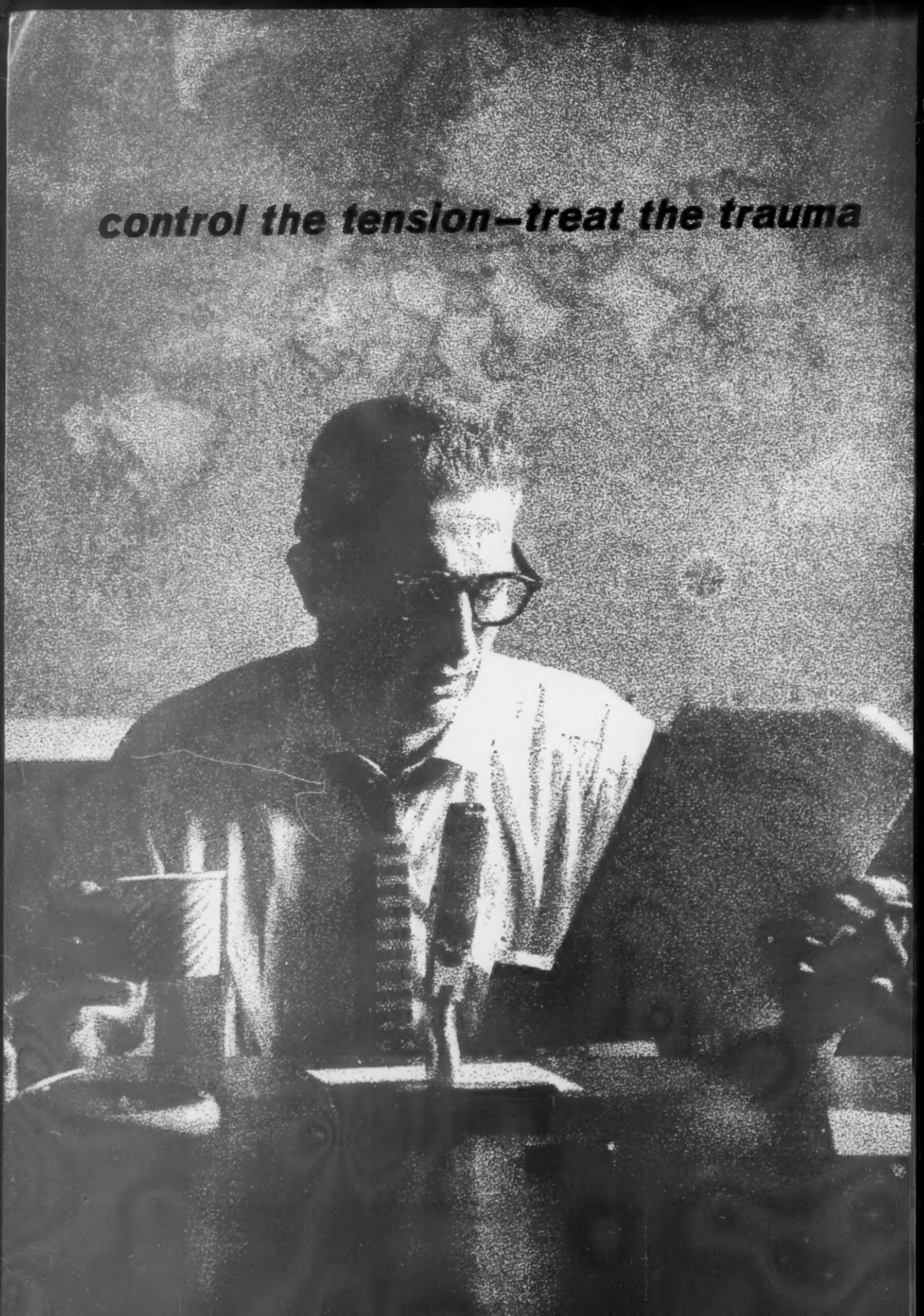
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being™


control the tension–treat the trauma

...Pathibamate® 400 200

meprobamate with PATHILON® tridihexethyl chloride Lederle

greater flexibility in the control of tension, hypermotility and excessive secretion in gastrointestinal dysfunctions

PATHIBAMATE combines two highly effective and well-tolerated therapeutic agents:

mebrobamate (400 mg. or 200 mg.) widely accepted tranquilizer and . . .

PATHILON (25 mg.)—anticholinergic noted for its peripheral, atropine-like action, with few side effects.

The clinical advantages of PATHIBAMATE have been confirmed by nearly two years' experience in the treatment of duodenal ulcer; gastric ulcer; intestinal colic; spastic and irritable colon; ileitis; esophageal spasm; anxiety neurosis with gastrointestinal symptoms and gastric hypermotility.

Two dosage strengths—PATHIBAMATE-400 and PATHIBAMATE-200 facilitate individualization of treatment in respect to both the degree of tension and associated G.I. sequelae, as well as the response of different patients to the component drugs.

Supplied: **PATHIBAMATE-400**—Each tablet (yellow, 1/2-scored) contains meprobamate, 400 mg.; PATHILON tridihexethyl chloride, 25 mg.

PATHIBAMATE-200—Each tablet (yellow, coated) contains meprobamate, 200 mg.; PATHILON tridihexethyl chloride, 25 mg.

Administration and Dosage: **PATHIBAMATE-400**—1 tablet three times a day at mealtime and 2 tablets at bedtime.

PATHIBAMATE-200—1 or 2 tablets three times a day at mealtime and 2 tablets at bedtime.

Adjust to patient response.

Contraindications: glaucoma; pyloric obstruction, and obstruction of the urinary bladder neck.

Lederle

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

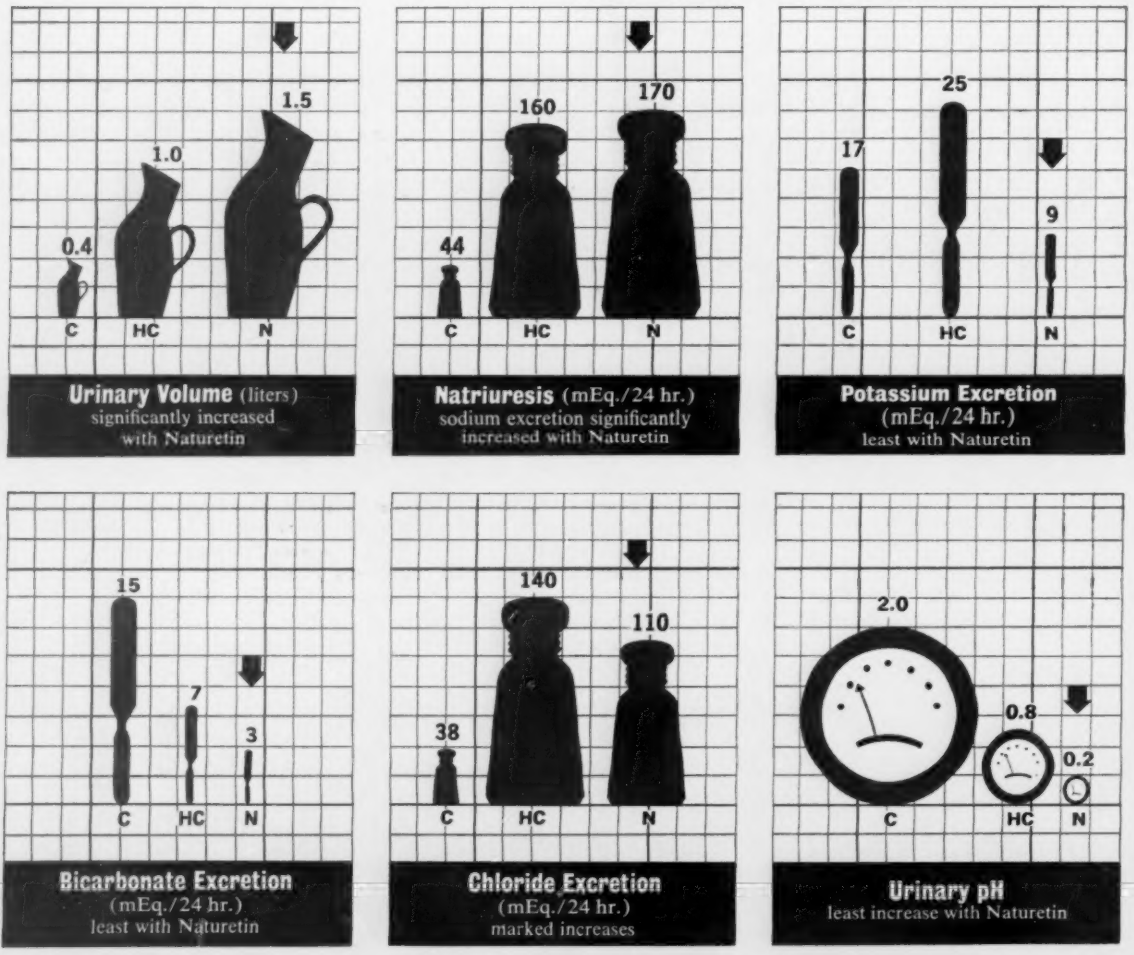
more closely approaches the ideal diuretic

Naturētin

Squibb Benzydroflumethiazide

"When compared to other members of this heterocyclic group of compounds, this drug [NATURETIN] shows a significantly increased natriuresis and decreased loss of potassium and bicarbonate. In this respect it more closely approaches a natural or 'ideal diuretic.' It is effective upon continuous administration and causes no significant serum biochemical changes. It is effective in a wide variety of edematous and hypertensive states and represents a significant advance in diuretic therapy." *Ford, R.V.: Pharmacological observations on a more potent benzothiadiazine diuretic; accepted for publication by the American Heart Journal.*

Comparison of electrolyte excretion pattern for the 24 hours following typical doses of chlorothiazide, hydrochlorothiazide, and Naturetin[1]



Typical Doses: Chlorothiazide—1,000 mg.; Hydrochlorothiazide—50 mg.; Naturetin (Benzydroflumethiazide)—5 mg.

1. Adapted from: Ford, R. V., Squibb Clin. Res. Notes 2:1 (Dec.) 1959.

A single 5 mg. tablet once a day provides all these advantages[2]

- prolonged action – in excess of 18 hours
- convenient once-a-day dosage
- low daily dosage – more economical for the patient
- no significant alteration in normal electrolyte excretion pattern
- repetitively effective as a diuretic and antihypertensive
- greater potency mg. for mg.—more than 100 times as potent as chlorothiazide
- potency maintained with continued administration
- low toxicity – few side effects – low salt diets not necessary
- comparative studies with chlorothiazide, hydrochlorothiazide, and Naturetin disclose that smallest doses of Naturetin produce greater weight loss per day
- in hypertension, Naturetin, alone or in combination with other antihypertensives, produces significant decreases in mean blood pressure and other favorable clinical effects
- purpura and agranulocytosis not observed
- allergic reactions rarely observed

[2]Reports (1959) to the Squibb Institute for Medical Research.

Naturētin – *Indications:* in control of edema when diuresis is required, in congestive heart failure, in the premenstrual syndrome, nephrosis and nephritis, cirrhosis with ascites, edema induced by drugs (certain steroids); in the management of hypertension, used alone, combined with Raudixin (Squibb Rauwolfia Serpentina Whole Root), or with other antihypertensive drugs, such as ganglionic blocking agents.

Contraindications: none, except in complete renal shutdown.

Precautions: when Naturetin is added to an antihypertensive regimen including hydralazine, veratrum, and/or ganglionic blocking agents, immediate reduction must be made in the dosage for all preparations; the dosage for ganglionic blocking agents must be decreased by 50% to avoid a precipitous drop in blood pressure. This also applies if these hypotensive drugs are added to an established Naturetin regimen . . . in hypochloremic alkalosis with or without hypokalemia . . . in cirrhotic patients or those on digitalis therapy when reductions in serum potassium are noted . . . in diabetic patients or those predisposed to diabetes . . . when increased uric acid concentrations are noted . . . when signs—leg or abdominal cramps, pruritus, paresthesia, rash—suggestive of hypersensitivity, are noted.

Naturētin – *Dosage: in edema,* average dose, 5 mg., once daily, preferably in the morning; to initiate therapy, up to 20 mg., once daily or in divided doses; for maintenance, 2.5 to 5.0 mg., daily in a single dose. *In hypertension:* suggested initial dose, 5 to 20 mg. daily; for maintenance, 2.5 to 15 mg. daily, depending on the individual response of the patient. When Naturetin is added to an antihypertensive regimen with other agents, lower maintenance doses of each drug should be used.

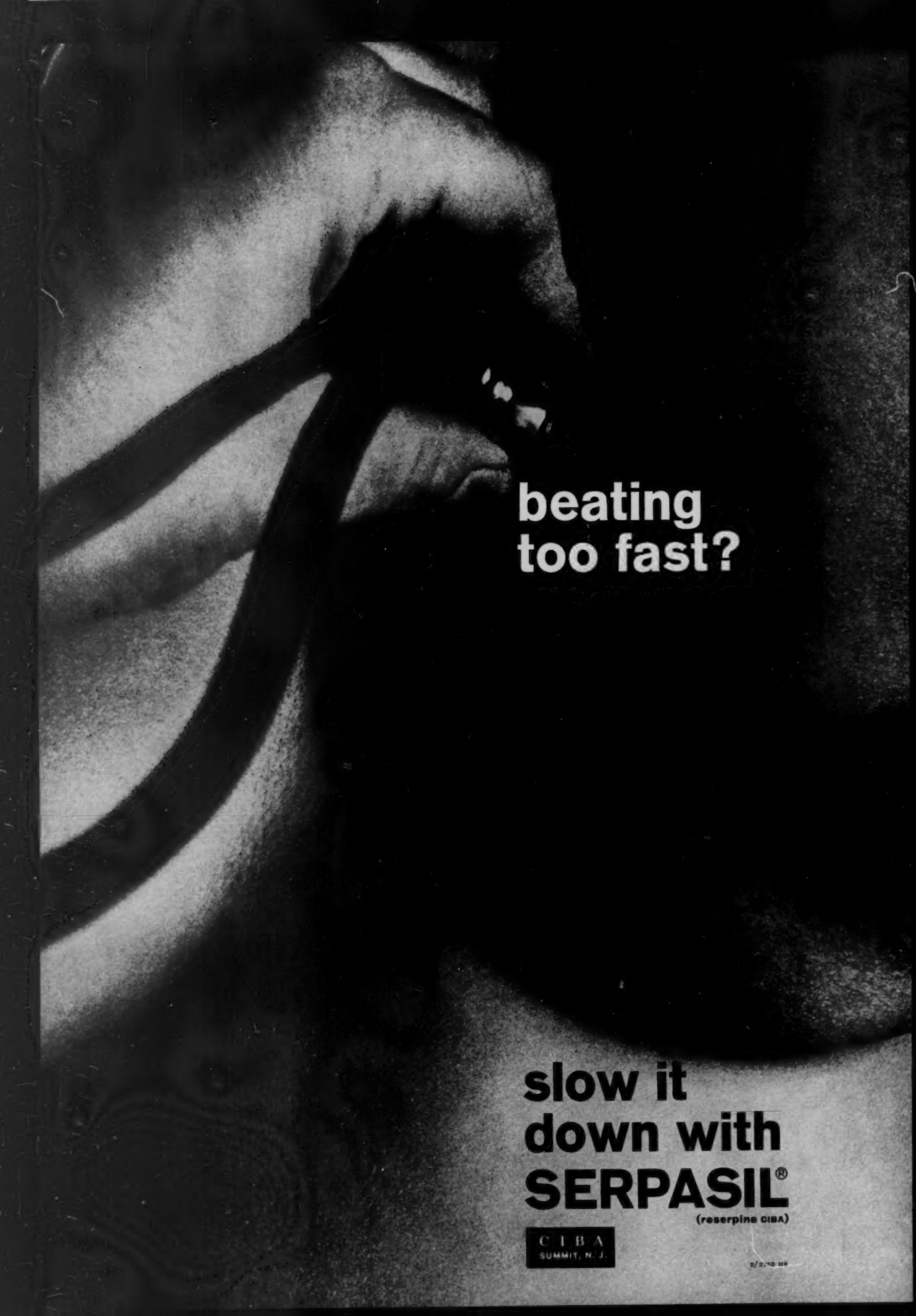
Naturētin – *Supplied:* tablets of 2.5 mg. and 5 mg. (scored).

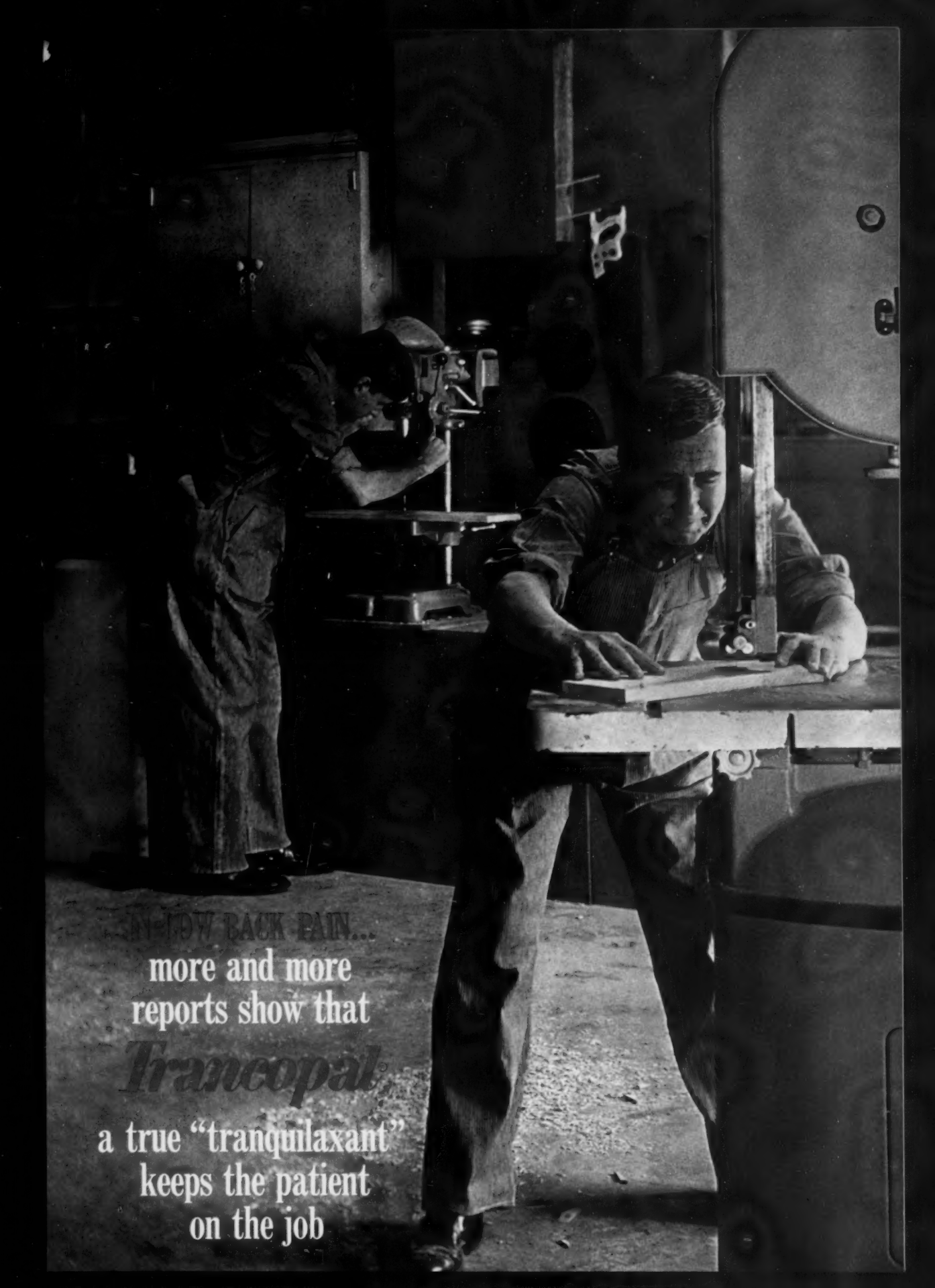
SQUIBB

Squibb Quality—the Priceless Ingredient

Rx Naturetin 5mg. Disp. #30 Sig: 1 each morning

'RAUDIXIN'® AND 'NATURETIN' ARE SQUIBB TRADEMARKS.


beating
too fast?
slow it
down with
SERPASIL®
(reserpine CIBA)
CIBA
SUMMIT, N. J.


IN LOW BACK PAIN...
more and more
reports show that
Trancopal
a true "tranquilaxant"
keeps the patient
on the job

THE FIRST TRUE "TRANQUILAXANT"

Trancopal®

relieves painful muscle spasm and relaxes the patient

Impressive numbers of patients with low back pain and other musculospastic conditions treated with Trancopal have been freed of symptoms and enabled to return to their usual activities, according to newly published clinical reports. In a recent study by Lichtman,[1] Trancopal brought excellent to satisfactory muscle relaxation to 817 of 879 patients. The patients in this group suffered from skeletal muscle spasm associated with low back pain (361 cases), stiff neck (128 cases), bursitis (177 cases), and other skeletal muscle disorders (213 cases). Side effects were rare (2 per cent of patients), and it was not necessary to discontinue medication in any of the patients. Lichtman comments: "Chlormethazanone [Trancopal] not only relieved painful muscle spasm, but allowed the patients to resume their normal activities with no interference in performance of either manual or intellectual tasks."[2]

When you prescribe Trancopal for musculoskeletal disorders, you can confidently expect that your patients will be relieved of the pain and stiffness. You can be sure of their speedy return to everyday work and recreation.

Mullin and Epifano call Trancopal "...a very effective skeletal muscle spasmolytic."[3] They found that Trancopal brought good to excellent relief to all of 39 patients with skeletal muscle spasm related to trauma, bursitis, rheumatoid arthritis, osteoarthritis, and intervertebral disc syndrome. (No side effects were noted except that one patient had slight dryness of the mouth.)

The pattern is similar in every new series reported: Ganz,[4] DeNyse,[5] Shanaphy[6] and Stough.[7]

Trancopal is a true "tranquilaxant"

Trancopal "...combines the properties of tranquilization and skeletal muscle relaxation with no concomitant change in normal consciousness."[6]

Relieves dysmenorrhea

Trancopal not only is valuable in treating patients with low back pain and other musculoskeletal disorders, but is also very effective in bringing relief from menstrual cramps and discomfort. Shanaphy suggests that Trancopal may help the patient by its combination of muscle relaxant and tranquilizing actions, and he finds that "...the continued use of chlormezanone [Trancopal] as a therapeutic agent in dysmenorrhea is advisable."[6] Trancopal was effective in 82 per cent of his series of 50 patients. In another study, which dealt with 52 adolescent girls and 23 women, Stough[7] reported that Trancopal gave complete or moderate relief in 86.4 per cent.

Alleviates tension

And, of course, Trancopal is also very useful in the treatment of patients in anxiety and tension states. As Ganz says, "...a most valuable drug for relieving tension, apprehension and various psychogenic states...allows the patient to use his energies in a more productive manner in overcoming his basic problems."[4]

Trancopal

a true "tranquilaxant"

that relieves skeletal muscle spasm and relaxes psychogenic tension without troublesome side effects, and keeps the patient on the job.

Indicated for...

Musculoskeletal disorders		Psychogenic disorders
Low back pain (lumbago)	Fibrositis	Anxiety and tension states
Neck pain (torticollis)	Ankle sprain, tennis elbow	Dysmenorrhea
Bursitis		Premenstrual tension
Rheumatoid arthritis	Myositis	Asthma
Osteoarthritis	Postoperative muscle spasm	Angina pectoris
Disc syndrome		Alcoholism

Now available in two strengths:

Trancopal Caplets®, 100 mg. (peach colored, scored), bottles of 100.

NEW STRENGTH ▶ Trancopal Caplets, 200 mg. (green colored, scored), bottles of 100.

Dosage: Adults, 100 or 200 mg. orally three or four times daily. Relief of symptoms occurs in from fifteen to thirty minutes and lasts from four to six hours.

References: 1. Lichtman, A. L.: Scientific Exhibit, meeting of the International College of Surgeons, Miami Beach, Fla., Jan. 4–7, 1959. 2. Lichtman, A. L.: *Kentucky Acad. Gen. Pract. J.* 4:28, Oct., 1958. 3. Mullin, W. G., and Epifano, Leonard: *Am. Pract. & Digest Treat.* 10:1745, Oct., 1959. 4. Ganz, S. E.: *J. Indiana M. A.* 52:1134, July, 1959. 5. DeNyse, D. L.: *M. Times* 87:1512, Nov., 1959. 6. Shanaphy, J. F.: *Current Therap. Res.* 1:59, Oct., 1959. 7. Stough, A. R.: *J. Oklahoma M. A.* 52:575, Sept., 1959.

Winthrop LABORATORIES
New York 18, New York

it started as a "cold"...

to prevent the sequelae of u.r.i. ... and relieve the symptom complex

ACHROCIDIN®

Tetracycline-Antihistamine-Analgesic Compound Lederle

Pneumonitis, otitis, tonsillitis, adenitis, sinusitis or bronchitis develops as a serious bacterial complication in about one in eight cases of acute upper respiratory infection.[1] To protect and relieve the "cold" patient...ACHROCIDIN.

Usual dosage: 2 tablets or teaspoonfuls q.i.d. (equiv. 1 Gm. tetracycline). Each TABLET contains: ACHROMYCIN® Tetracycline (125 mg.); phenacetin (120 mg.); caffeine (30 mg.); salicylamide (150 mg.); chlorothen citrate (25 mg.). Also as SYRUP (lemon-lime flavored), caffeine-free.

1. Based on estimate by Van Volkenburgh, V. A., and Frost, W. H.: Am. J. Hygiene 71:122 (Jan.) 1933

Lederle LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

When you want to prescribe a diet to lower serum cholesterol, is a low-fat low-cholesterol diet the best way?

No, not according to today's thinking. A more efficient way is to control the type and amount of fat in the diet.

This means to control the total calories and to replace the saturated fats wherever possible with poly-unsaturated vegetable oil.

There is a considerable agreement among heart research workers that a low-fat diet does not by itself consistently reduce beta lipoproteins and blood cholesterol or sustain a low level. Many low-fat diets merely eliminate the visible fats. The *invisible* fat, inherent in meat and dairy products, is basically *saturated fat*, so that a low-fat diet quite frequently is actually relatively high in saturated fat. Consequently, the patient does not get the proper percentage of the *poly-unsaturated fatty acids* that help to lower blood serum cholesterol and to maintain it at proper levels.

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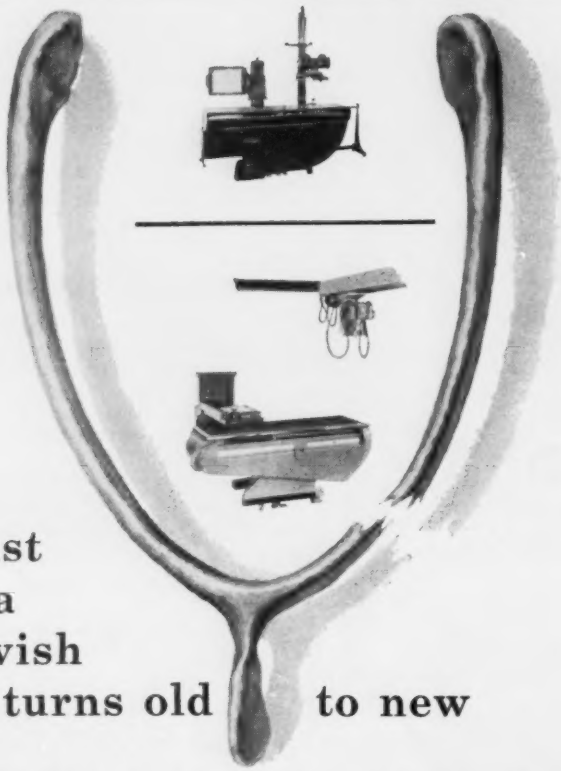

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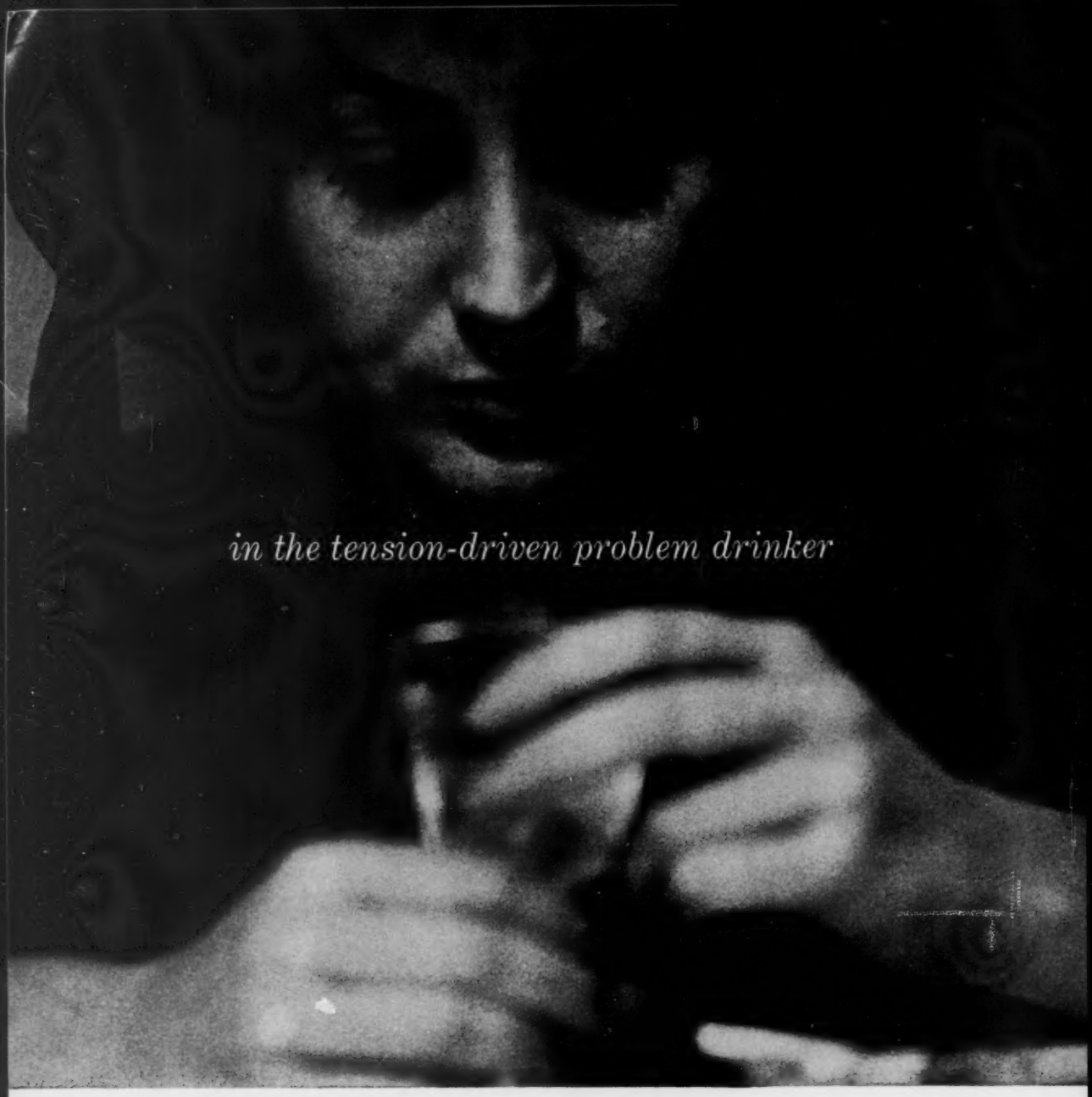

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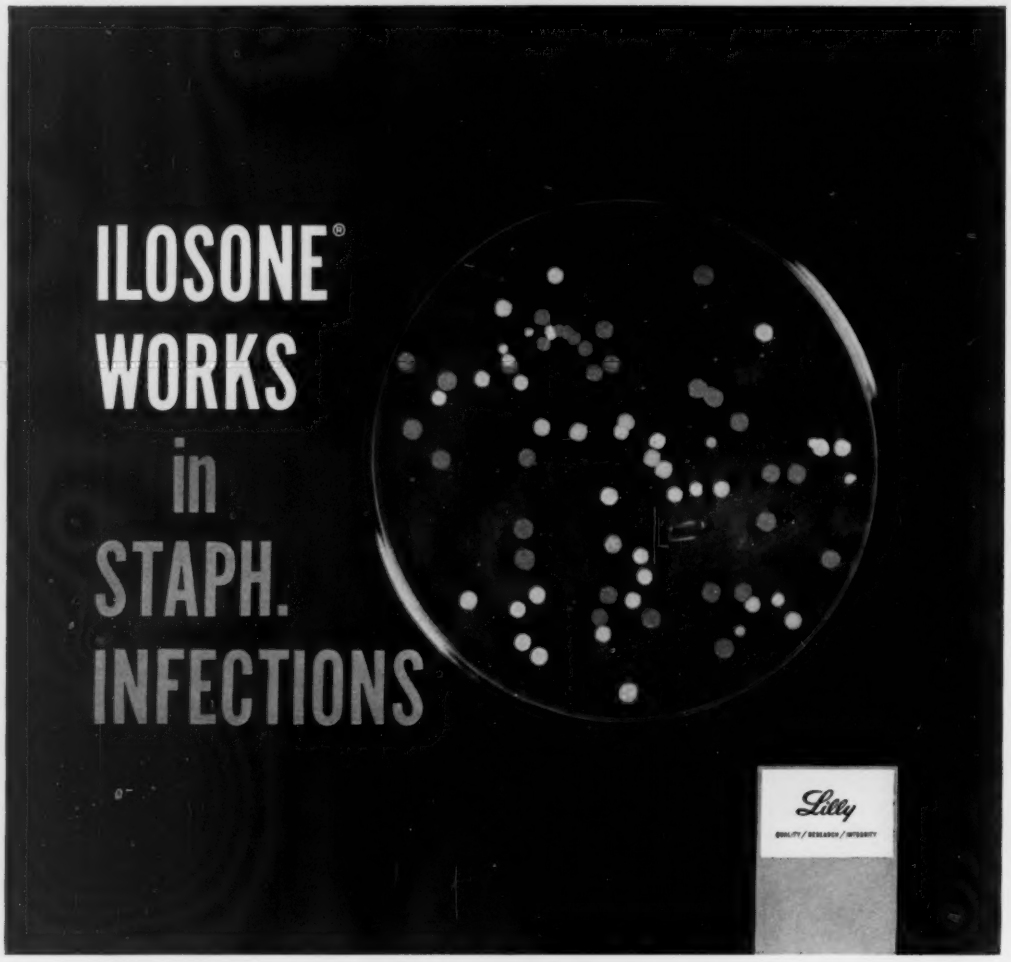

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NORTH CAROLINA MEDICAL JOURNAL

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VOLUME 21 JANUARY, 1960 NO. 1

Roentgen Changes in Salmonella Osteomyelitis Occurring in Children With and Without Sickle Cell Anemia*

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CHAPEL HILL

Involvement of the skeletal system is an unusual but well recognized complication of salmonellosis. Recent clinical reports suggest that patients with sickle cell anemia are predisposed to the development of osteomyelitis caused by a variety of bacteria, and by the Salmonella genus in particular. Certain radiologic changes in patients with osteomyelitis complicating sickle cell anemia have been described as unique. It is the purpose of this paper to describe 3 patients with Salmonella osteomyelitis treated recently at the North Carolina Memorial Hospital and to attempt to evaluate in each of these the worth of radiologic changes in diagnosis.

Incidence and Pathology

The Salmonella group comprises a variety of paratyphoid organisms—more than 150 species—which ordinarily are intestinal parasites. Bacteremia occurring in salmonellosis is, however, quite common and has become a principal means of diagnosis. The blood-borne infection may result in the development of a septic process in any organ. Paratyphoid osteomyelitis is somewhat less frequent than bone infection following typhoid fever, but once established, may be the more virulent[1]. Osteomyelitis subsequently develops in approximately 1 per cent of patients having typhoid fever[2], while skeletal involvement occurs in only 0.2 per cent of the cases of paratyphoid fever[3]. In a breakdown by age groups, however, of 1,497 cases of Salmonella infections at the New York Salmonella Center, Seligman[4] found that 17 per cent were in infants and 40 per cent were in children under 10 years of age. Osteomyelitis and arthritis were found in 20 per cent of the children under 2 years of age when *Sal. choleraesuis* was the offending organism.

The skeletal lesions of paratyphoid infections may exhibit pathologic features which distinguish them from the more frequently occurring staphylococcal and streptococcal lesions, and even from those associated typhoid infection. The lesions are multiple in many instances. Involvement of the bones of the shoulder girdle, ribs, spine, and long bones, particularly of the upper extremities, has been reported most frequently. Inflammation usually begins beneath the periosteum in the diaphyseal portion of the bone rather than in the metaphysis. The earliest change is thickening and elevation of the periosteum of the shaft, resulting from periostitis. If the lesion remains localized, nonsuppurative and sclerosing osteitis of the adjacent bone may occur. The process is more likely to spread throughout the bone, and once diffuse suppuration has developed, there is no reliable way of pathologically distinguishing Salmonella osteomyelitis from changes resulting from staphylococcal or streptococcal infections. Bacterial invasion of the joint may also involve the bone. Suppurative arthritis ordinarily precedes osteomyelitis in these instances, with destruction of the synovial membrane, cartilage, and eventually bone. The infections are usually monarticular, and large joints are more often affected.

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Sickle cell anemia is a familial chronic hemolytic disease characterized by the generation of abnormal hemoglobin with resultant sickle-shaped erythrocytes under certain conditions. The abnormal erythrocytes are destroyed prematurely by the reticuloendothelial cells, and compensatory hyperplasia of the blood-forming organ occurs. The result in the skeleton, early in life, is overgrowth of marrow, causing dilatation of the medullary cavity and atrophy of the spongiosa and corticalis from pressure. Infarction of the bones is common, particularly in children.

Bone infections, generally, are more common in patients with sickle cell anemia than in normal individuals[5]. During the last 10 years several cases of Salmonella osteomyelitis complicating sickle cell anemia have been reported in the literature (Burch[6], Wigh and Thompson[7], Hughes and Carroll[8] 1957, and Lohmuller and Marshall[9]). In all, approximately a dozen instances of concurrence of the diseases have been recorded.

Roentgenologic Investigation

The roentgenographic changes occurring in one case of osteomyelitis complicating sickle cell anemia were well described in detail by Wigh and Thompson[7]. They noted that the diaphyses rather than the juxta-epiphyseal regions were infected initially, in accord with the observations of others (Burch), MacDonald, Veal, and Veal and McFetridge).

A distinctive feature pointed out by Wigh and Thompson[7] was the presence of linear intracortical fissuring paralleling the shaft adjacent to the medullary involvement. The length of the fissuring was the same as the extent of the medullary disease. There were short intraosseous sinus tracts between the obvious medullary infection and the cortical fissure. The fissuring was clearly defined as lying between cortex and endosteal limits; it did not represent uncalcified matrix between new subperiosteal bone and cortex.

Fig. 1. Salmonella osteomyelitis complicating sickle cell anemia. Bone destruction is present throughout the entire shaft of the left radius. A well developed involucrum is present, indicating late stages of bony involvement with the rebuilding process well established. A pathologic fracture is shown in the distal radius (Same case as Fig. 2.)

Other frequently observed roentgen findings are: (1) multiple bone involvement, (2) irregular areas of destruction, (3) extensive periosteal proliferation, (4) involucrum formation, and occasionally, (5) pathologic fractures.

Material

The material available for study consists of 3 patients with Salmonella osteomyelitis verified by bacteriologic culture from the diseased tissues. All of the patients were children below the age of 15 years. Two patients (cases 1 and 2) had clinical manifestations of sickle cell anemia, and the diagnosis was confirmed by electrophoresis. Both patients had hemoglobin type "S", specific for the anemia and not the trait. In these patients the osteomyelitis developed in the long bones of the upper extremities, providing adequate opportunity to observe osseous and particularly cortical changes. One of these 2 patients also

Fig. 2. A film of the right forearm (A) shows extensive cortical involvement of the diaphysis of a long bone (radius). There is early cortical fissuring in the distal right humerus (arrow). A small draining sinus (arrow) is seen to perforate the periosteum of the radius. (Same case as Fig. 1.) A film made two months later (B) reveals almost complete healing.

had vertebral disease. In the third patient, who did not have sickle cell anemia (normal hemoglobin type "A"), skeletal infection developed first in the knee joint as a suppurative arthritis, and osteomyelitis of the adjacent tibia was secondary to the joint disease.

Case 1 (figs. 1 and 2)

A 4 year old Negro girl was admitted to the North Carolina Memorial Hospital because of fever, pain, and swelling in both elbows of 17 days' duration. She had anemia with 6 Gm. of hemoglobin and a hematocrit value of 20. A sickle cell preparation was positive and electrophoretic studies showed hemoglobin type "S". **Sal. bareilly** was cultured from the elbow-joint aspirate. Radiologic examination revealed alteration of bony density and architecture suggestive of osteomyelitis of the right humerus, both radiuses, and both ulnas. Other bones were normal.

A lateral radiograph of the left forearm (fig. 1) shows destruction throughout the entire shaft of the left radius. A pathologic fracture is noted in the distal radius. The partially destroyed shaft is seen to be encased in a well developed involucrum, indicating late stages of bony involvement, with the rebuilding process well established.

A film of the right forearm (fig. 2A) shows similar changes, somewhat less marked, and illustrates well the extensive cortical involvement of the diaphysis of a long bone. There is evidence of beginning cortical fissuring in the distal right humerus. A small draining sinus in the proximal radius is seen to perforate the periosteum. A film made two months later (fig. 2B) revealed a considerable degree of healing.

Case 2 (figs. 3 and 4)

A 14 year old Negro boy was admitted to the pediatric service because of fever, multiple joint pains, and exercise intolerance. The patient had icteric conjunctivae and soft tissue swelling of the left elbow, with marked tenderness and limitation of motion. Anemia was present, with a hemoglobin of 8.2 Gm. and a hematocrit of 24. Electrophoretic studies revealed type "S" hemoglobin. A heavy growth of **S. choleraesuis** was cultured from the venous blood and left elbow joint aspirate. Initial radiologic examination revealed a destructive process involving the left forearm and changes of hematopoietic disease in the spine, but no evidence of collapse or infection.

A film of the left forearm (fig. 3) revealed multifocal destructive areas in the upper portion of the shaft of the radius and ulna. Marked proliferative periosteal reaction is present and cortical fissuring is a prominent finding.

Fig. 3. Salmonella osteomyelitis complicating sickle cell anemia. The left elbow exhibits multifocal destructive areas in the upper portion of the shaft of the radius and ulna. Marked proliferative periosteal reaction is present and cortical fissuring (arrow) is a prominent finding. (Same case as Fig. 4.)

Films of the thoracolumbar spine (fig. 4A) made eight weeks after admission revealed the development of a destructive process involving the thoracic 12, lumbar 1 and lumbar 2 vertebrae. Earlier films showed the classic ballooning of the disc spaces, with a generalized decrease in density of the centra prior to the vertebral collapse. Films made three weeks later after recovery (fig. 4B) show bony sclerosis and healing without evidence of progression of the destructive process. No bacteriologic studies were made from this region.

Case 3 (fig. 5).

A 6 month old Negro female infant was admitted to the pediatric service because of a painful, tender, swollen right knee. During hospitalization **Sal. choleraesuis** was cultured from turbid fluid removed from the right knee joint. There was only a mild nutritional anemia and several sickle cell preparations revealed no abnormal ery-

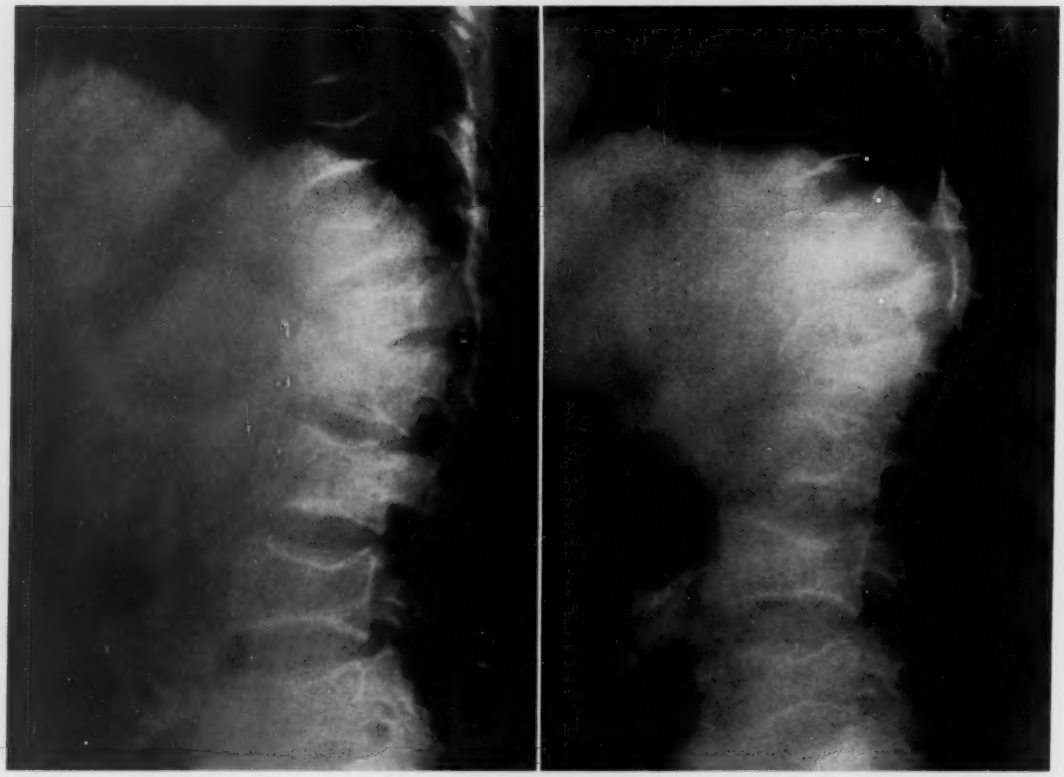

Fig. 4. The thoracolumbar spine shows a marked destructive involving T-12, L-1 and L-2 with vertebral collapse (A). There is narrowing of the intervening disc spaces characteristic of an infectious process. A film made three weeks later (B) shows bony sclerosis and disc space bridging indicating healing without further evidence of destruction. (Same case as Fig. 3.)

throcytes. Electrophoretic studies showed a normal hemoglobin, type A. There was no history of blood transfusions. The child did not appear ill at any time.

Films of the right knee (fig. 5) showed soft-tissue swelling, joint effusion and scattered areas of subchondral bone destruction in the proximal epiphyseal center of the tibia. There is subepiphyseal lysis of bone in the proximal end of the tibia, with minimal evidence of periosteal new bone. A moderate-sized radiolucent defect is noted in the anteromedial aspect of the tibial metaphysis.

Comment

We have taken this opportunity to study and compare 3 cases of Salmonella osteomyelitis, 2 of which were complications of sickle cell anemia. This summary is presented as further support of previous observations by Hodges[10], Hughs and Carroll[8], and Lohmuller and Marshall[9] that Salmonella osteomyelitis complicating sickle cell anemia probably is more than coincidental.

The predisposition of the infectious process to involve predominantly the diaphysis rather than the metaphysis, and intracortical fissuring parallel to the long axis of the involved bone are illustrated, and may well be valid as specific diagnostic aids in roentgen examinations done fairly early in the disease.

Only a limited number of cases throughout the literature have been available for review, but specific and similar findings are being described constantly. A striking difference is seen between the bone changes in our 2 patients with both diseases and those in the child who had Salmonella osteomyelitis in the absence of sickle cell anemia.

Some disagreement has arisen regarding the opinions expressed by Rowe and Haggard[11], who reported 2 cases of bone changes in children with sickle cell anemia. *Sal. typhimurium* was cultured from an ab-

Fig. 5. Salmonella arthritis and secondary osteomyelitis. Radiographs of the right knee (A & B) show joint effusion and scattered areas of subchondral bone destruction in the proximal epiphyseal center of the tibia. There is subepiphyseal lysis of bone in the proximal end of the tibial metaphysis with minimal evidence of periosteal new bone.

scess on the hand in 1 case. The authors believed that the abnormal bone picture was not related to the Salmonella organism but due rather to infarction alone. While bone infarction may be a predominant factor in producing pathologic bone changes in uncomplicated sickle cell anemia, other investigators do not share the view that the extensive changes accompanying salmonellosis can be explained other than by the presence of septic bone disease. This is also our belief, since in 2 of the cases presented in this paper salmonellal osteomyelitis complicating sickle cell anemia was definitely established and the unique bone changes which have been described by others in this combination of diseases are validated.

Summary

Three cases of Salmonella osteomyelitis occurring in Negro children are reported. Sickle cell anemia was proved to be present in 2 of the cases. The skeletal changes occurring in these cases give further support

to the opinion that children with sickle cell anemia have a predisposition to osteomyelitis and that there is a striking tendency for paratyphoid organisms to be the offending agents. The roentgen characteristics of polyostotic involvement, particularly of the upper extremities, diaphyseal predilection, extensive periosteal proliferation, and longitudinal fissuring of the cortex of tubular bones are further substantiated.

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The Cornell Medical Index Health Questionnaire as a Diagnostic Aid

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CHAPEL HILL

The absolute necessity of a complete clinical history in the adequate evaluation of patients is well recognized. However, this part of the work-up is quite time consuming and any procedure which would shorten the time required without reducing the quality of the history would be a useful adjunct to patient care. The use of the Cornell Medical Index Health Questionnaire in ambulatory patient care has been well described by Brodman and others[1] and Erdmann[2]. The present study was undertaken to discover if this questionnaire would be of value in improving the completeness of clinical histories as obtained in a teaching hospital out-patient department.

Procedure

During the summer of 1959 a copy of the Cornell Medical Index-Medical Questionnaire (CMI) and an explanatory letter were mailed to 92 consecutive patients who had been given their first appointments for complete medical evaluation in the General Clinic of the North Carolina Memorial Hospital. The accompanying letter explained the purpose of the form and requested that it be returned at the time of the clinic visit. Twenty-two of these patients cancelled or failed to come in for their appointments. Thus 70 patients (76 per cent) who were mailed CMI's came in for diagnostic work-up. Of this number, 56 patients (80 per cent) returned with the forms completed, which means that 60 per cent of the original 92 CMI'S were recovered for study.

When the form was received by the clinic secretary it was delivered directly to the author, so that it was not used in the clinical evaluation of the patient. Each form was then studied and tentative clinical impressions were recorded. These impressions were usually coded as tentative diagnoses, but in some instances they were coded simply as "systems requiring careful study." The CMI's were further examined for evidence of emotional disturbance on the basis of the total number of positive answers, as well as the positive answers to certain specific questions designed to bring out evidence of psychopathologic disorders.

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After this portion of the study was completed, and some weeks after these patients were first seen, their clinical records were examined from the standpoint of diagnoses made, pertinent points in the history indicated on the CMI but not mentioned on the clinical work-up, diagnoses made clinically which were not suggested by the CMI, and, finally, the emotional evaluation of the patient from the CMI as compared with that made by the examining physician and recorded on the clinical record.

Results

As a result of this comparison, it was determined that in 51 patients (90 per cent) the primary diagnosis was correctly indicated by the CMI, at least by system. In 5 (10 per cent) the diagnosis was missed by the CMI. The five diagnoses missed included functional heart murmur, glaucoma, anxiety reaction, cardiac neurosis, and nontoxic, benign thyroid nodule (table 1).

The CMI correctly indicated the system in which the secondary diagnosis occurred in 29 of the 35 secondary diagnoses made. Twenty-one charts contained no secondary diagnosis. Thus in 83 per cent of the secondary diagnoses the correct system was indicated by the CMI. Secondary diagnoses which were not indicated included mental deficiency (2 cases), benign prostatic hyperplasia, hypertensive cardiovascular disease with congestive heart failure (in a patient with carcinoma of the lung), and neurologic deficit of the left leg of unknown etiology.

On 13 charts a third diagnosis was recorded and in all 13 instances this diagnosis had been indicated by the CMI. The majority were such diseases as varicose veins, benign prostatic hyperplasia, and obesity.

In 21 of the 56 clinical records (38 per cent), a significant emotional element in the patients' problems was noted. In 2 of these, this element was not detected by the CMI. On rereading these two CMI's, however, it was apparent that one of the patients presented evidence of hysterical symptomatology by volunteering a considerable amount of information which was not requested, and by having a large total of positive answers. The fact that a number of these positive answers concerned the cardiovascular system led to the erroneous impression (from the CMI) that she had heart disease, whereas the clinical diagnosis was cardiac neurosis.

Table 1

Use of the Cornell Medical Index-Questionnaire With 92 Consecutive Patients

Total CMI's mailed	92
No. patients keeping appointment for work-up	70
No. of CMI's returned	56 (80%)
Detection of primary diagnosis by CMI	90%
Detection of secondary diagnosis* by CMI	83%
Detection of third diagnosis* by CMI	100%
Possible "Missed diagnosis" detected by CMI	15 (26%)
Emotional problems recognized on clinical evaluation	38%
Emotional problems indicated by CMI's	70%

*Applicable where a secondary or third diagnosis was present.

According to the CMI, 38 of the 56 patients had significant emotional problems (70 per cent as compared with 38 per cent from the clinical studies). Most of these patients gave positive answers to such questions as, "Do you get nervous and shaky when approached by a superior?"; "Do you usually feel unhappy and depressed?"; "Do you often cry?"; "Do you often wish you were dead and away from it all?"; "Are you always in poor health?"; "Are you always ill and unhappy?", and others in this vein. It is suspected that these patients have emotional problems which were overlooked during their clinical examinations. This is not to say that the emotional problem represented the primary diagnosis, because in the majority of cases it most likely did not. In order to understand a patient's illness, however, these factors are of obvious importance.

In this group of 56 cases, a total of 15 (26 per cent) organic diagnoses, all of at least potential importance to the patients, were suggested by the CMI's but not noted on the clinical history. These included hemorrhoids in 2 patients: arthritis and varicose veins in 1; varicose veins in 1; epilepsy in 2; deafness in 1; alcoholic intake and a history of jaundice in 1; a history of probable syphilis in 1 (later confirmed by a positive VDRL); a draining ear with decreased hearing in 1; a history of worms with a clinical finding of 7 per cent eosinophilia and no stool studies in 1; vaginal discharge in 1, with no pelvic examination recorded; a history of rheumatic fever in

1 patient, who was found on examination to have a mitral systolic murmur believed by the examiner to be functional; bladder symptoms in 1 patient with pyuria on urinalysis, which was not further treated or evaluated; nasal allergy in 1; and symptoms strongly suggestive of peptic ulcer in 1 patient on whom review of systems was recorded as "GI negative."

Comment

Those who have worked most intensively with the Cornell Medical Index-Health Questionnaire are impressed with its value as an adjunct to comprehensive evaluation of patients[3]. It is easily administered and can usually be completed in less than 30 minutes by a patient who has had an elementary education. Other patients may require help, which can frequently be given by a relative. In the present study all except one of the CMI forms submitted were properly completed, and in that one the questions that were answered correlated well with the clinical history.

This study tends to confirm the impression that the CMI serves to give a more comprehensive review of systems, as well as to provide insight into the emotional and personal problems of patients which otherwise is difficult to obtain. This is particularly true in the evaluation of new patients. Thus it would seem that this instrument should be widely applicable in office and and clinic practice. It should also be useful in obtaining more complete medical records in community hospitals. The fact that this type of medical information is easily obtained and quickly evaluated by the physician should result in better patient care where it is used to complement a carefully taken clinical history.

Summary

The results of a comparative study of tentative diagnoses made by means of an evaluation of Cornell Medical Index-Health Questionnaires and clinical evaluations made independently have shown that the CMI indicates the area of the patient's major medical problems in the majority of instances, and points out minor medical and emotional problems which might otherwise be overlooked. It would therefore appear to have wide usefulness in medical practice.

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The depressive episodes may vary greatly in intensity. The mildest varieties may be unrecognized clinically and may appear only as periods of inertia or "staleness." The patient may complain merely of fatigability and a lack of ambition with an unexplained difficulty in concentrating his attention on tasks at hand. He may worry about matters that previously he had been able to resolve without difficulty. His family may relate that he has become stubborn, peevish and fault-finding. Physically he may complain of anorexia, loss of weight and disturbed sleep. The most typical variety of insomnia is that of early morning awakening and sleeplessness for the two or three hours before the accustomed time of arising. The patient usually believes that his disorder is of organic origin and that his downheartedness is the natural result of his ill health. Too often such patients are subjected to well-meaning but useless "treatment" with vitamins, hematinics and a variety of sex hormones. Barry, M.J., Jr., and Faucett, R. L.: The Depressed Patient, Proc. Staff Meet., Mayo Clin. 34:88 (Feb. 18) 1959.

The Tissue Committee In A General Hospital

LEDYARD DECAMP, M.D.
CHARLOTTE

In the summer of 1952, following recommendations of our pathologist, a Tissue Committee was appointed by the executive committee of the staff of Presbyterian Hospital in Charlotte. The primary reason for this action was (1) to encourage staff members to maintain more complete and detailed records of surgical patients, and (2) to comply with recommendations of the Joint Commission on Accreditation of Hospitals.

The Tissue Committee has usually consisted of the following: a member of the Department of Internal Medicine as chairman; a general surgeon or urologist; an obstetrician and gynecologist; a pathologist, and a radiologist. In the first two years of its existence the Committee met twice a month, but in the last four and a half years it has not had to meet more than once a month, as the number of charts to be reviewed has steadily dropped.

The hospital charts selected for review were those in which some discrepancy between preoperative and postoperative diagnoses, a discrepancy between the clinical and pathologic diagnoses, or both were noted by the chief of the Department of Pathology. Over the six and a half years span of this survey, between 80 and 85 per cent of all the charts studied were found to be satisfactory on close scrutiny (table 1). A number of records studied were considered to be incomplete in certain respects, and were referred to the Record Committee for completion. This number averaged 18 per cent in the first two years, falling to approximately 11 per cent in the last three years of this study.

A final group were those charts in which the clinical and pathologic diagnoses were at wide variance or indications for surgery were felt to be inadequate following the submission of additional data by the attending physician. In the first two years of the survey this category averaged 25 per cent of all charts reviewed and dropped to a little more than 7 per cent in the last three years of our study.

From Presbyterian Hospital, Charlotte, North Carolina.

Table 1

Experience of Tissue Committee

	Average Number Each Six Months		Per Cent	
	First Two Years	Last Three Years	First Two Years	Last Three Years
Charts reviewed	84	21		
Charts found satisfactory	72	33	85.7	80
Incomplete charts	15	4.6	18	11
Charts showing questionable indications for surgery	21	3	25	7.3

Every referred chart in the latter category was accompanied by a brief note expressing the Committee's views and requesting additional information which might have any direct bearing on the case. This step frequently led to the submission of additional history, summaries of office treatments, and so forth, which placed an entirely different light on the procedure performed and justified re-classifying the record as satisfactory.

The Tissue Committee has functioned in an advisory capacity entirely, and reports its findings to the executive committee of the staff. It was originally intended that any disciplinary measures would be taken by the executive committee. In the six and a half years of operation no member of the staff has had to be disciplined for repeated ill advised or unnecessary surgery.

In its first years of operation an occasional staff member took issue with the Tissue Committee's comments or recommendations. A year of membership on the Committee gave these physicians a clearer insight into the problems of evaluating the managment of a controversial case, and helped to show that the value of a record depends upon what is recorded in it, rather than on office notes.

Figure 1 graphically summarizes the results of the Tissue Committee's experience over the period from August, 1952, to March, 1959. It might be worth mentioning that in the last year of this survey there was an increase in bed capacity from 280 to 402 and almost a 40 per cent increase in the amount of surgery done. In

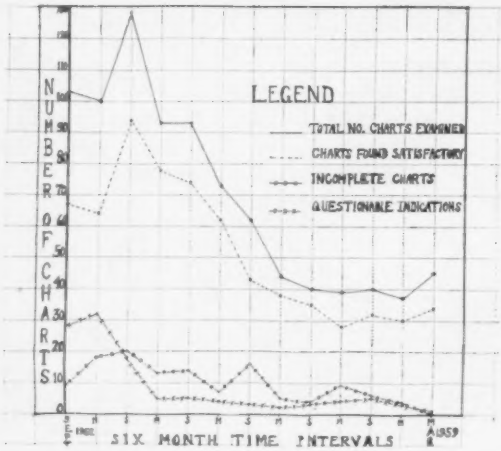

Figure 1

spite of this increase, the number of incomplete records or unjustified operations has dropped to almost zero.

Conclusions

It is believed that the two most important contributions that can be made by a conscientiously functioning Tissue Committee in a non-teaching general hospital are the following;

1. The improvement of perfunctory and incomplete records by filling in additional details of the patient's illness and past medical history that have a direct or an indirect bearing on the operation performed.
2. The reduction of the number of ill advised or hasty operations performed on the basis of perfunctory or inadequate preoperative studies by requiring staff surgeons to give reasonable justification for whatever procedure is done on each hospital record.

Discussion

Dr. C. T. Daniel (Fayetteville): This is a timely subject, for I feel that much can be done to improve the tissue committee in many of our hospitals. I wholeheartly agree on the conclusions reached by the author; namely, that improved records lead toward improved practice, with fewer instances of unwarranted or ill-advised surgery.

The reaction to a tissue committee is quite variable. It is assumed that the majority of doctors are competent and strive to give the best possible care to a patient. It is also evident that most doctors tend to resent any form of restrictive supervision of their activities. The tissue committee must strive to avoid personality clashes and conduct itself in such a manner that its purpose can be accomplished without causing ill will.

I would like to mention a few points that I feel contribute to the efficiency of our tissue committee. Rather than have the pathologist screen our charts for discrepancies, we utilize the clinicians on the committee who are better suited to evaluate a case as a whole. There are many cases in which the clinical and pathologic diagnoses agree, but the procedure performed is questionable.

The function of the tissue committee as an educational tool is stressed. Well managed cases of general interest are often presented during a session. At the present time we are trying a plan that is aimed at leaving the name of the operator out of the discussion if he desires. When a chart is to be presented, the physician is notified and given an opportunity to discuss the case with the committee prior to the staff meeting. The case is then presented by a qualified member of the committee, utilizing the material available in the record and supported by data from the recent literature in his discussion.

One of the objections voiced by critics of the committee has been that cases brought up for discussion usually resolve into discussion of gynecologic procedures.

In reviewing our records for the past year, I found that 72 per cent of the tissues studied were from gynecologic patients. Approximately half of these patients were operated on by doctors other than gynecologists. It was encouraging to note that the uterine suspensions, bilateral salpingectomies, exploratory laparotomies, and therapeutic abortions had been reduced to a minimum. I have little doubt that a tissue committee made up of qualified, conscientious members can do a great deal toward raising our surgical standards.

No prescription should ever leave the physician's hands unless it is dated and explicit directions regarding dosage, method of administration and refills are given. The term "as directed" should never be used. These simple steps are essential if the physician is to protect his patient properly.—Friend, D. G.: Polypharmacy—Multiple-Ingredient and Shotgun Prescriptions, New England J. Med. 260:1017 (May 14) 1959.

Non-Hormonal Adrenal Cortical Carcinoma

A Case Report

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and
W. RALPH DEATON, JR., M.D.
GREENSBORO

Primary tumors of the adrenal cortex are quite rare, and adrenal cortical carcinomas, which are non-hormonal and as such produce no evidence of glandular effect, are the rarest of all. (Cahill and Melicow's[1] classification is helpful in placing such tumors in perspective with other tumors of the adrenal gland.) Unfortunately, the non-hormonal tumors are also among the most malignant of all tumors, and in the majority of the reported cases the diagnosis has been made only after metastases have developed. Wood and others[2], in a survey of the European and American literature from 1923 to 1957, were able to find reports of only 27 cases wherein the diagnosis had been made before metastases occurred. The metastases have typically invaded the soft tissues—namely, the retroperitoneal lymph nodes, the liver, and the lungs, usually in that order. Death usually ensues within a year after metastasis occurs or is discovered. Heinbecker and others[3] out of 10 cases of cortical carcinoma could report only one patient alive, and this only 10 months after the operation. Their longest period of survival was three years.

The case described in this report differs from those which have been reported previously in two respects; (1), the longevity of the patient after the disease was discovered, and (2) the pattern of the metastases.

Case Report

The patient, a white man, was first seen at the age of 41 because of a urinary tract infection. Examination at that time revealed a movable mass approximately the size and shape of a large orange, and visible on x-ray examination of the abdomen, under the left subcostal margin; the patient had been previously unaware of the mass. He was treated successfully for the urinary infection, but refused laparotomy for removal of the mass.

From the Medical and Surgical Services of the Moses H. Cone Memorial Hospital, Greensboro, North Carolina.

He was seen three years later by another physician for right ureteral calculus. The record contains no mention of the mass in the left upper quadrant. Albumin and red blood cells were present in the urine. An intravenous pyelogram revealed hydronephrosis on the right, but no abnormality in the region of the left kidney was seen on the x-ray films. The blood calcium was 9.4 mg. per 100 cc., and the phosphorus was 2.4 mg. per 100 cc.

His next examination was a year later, when he complained of headache, vomiting, and pain in the left lower quadrant of the abdomen. On this occasion the mass in the left upper quadrant was again identified. Blood pressure was 110 systolic, 80 diastolic. Six months later, or four and a half years after the mass was first discovered, the patient, now 45 years old, complained of episodes of fainting, and a weight loss of 20 pounds. He had been working in a steel mill at hard physical labor, and except for the illnesses described above had been well. A nontender firm, grapefruit-sized mass (roughly 15 cm. in diameter) which moved with respiration was present in the left upper quadrant. Blood pressure was 140 systolic, 90 diastolic. Laboratory studies revealed microscopic hematuria, a flat glucose tolerance curve, an eosinophil count of 176 per cubic millimeter, a negative spinal puncture, normal hemogram, sedimentation rate of 8 millimeters per hour, and a normal intravenous pyelogram. The barium-filled stomach was seen to be displaced cephalad and medially by the mass when the patient was in the prone position.

On exploratory laparotomy a spherical solid tumor was found attached to the lower pole of the left adrenal gland. The entire gland and tumor were removed together. The pathologic report (H. L. Lennon, M.D.) stated that the specimen was a smooth rounded encapsulated mass, 11.5 cm. in diameter. On cut section (fig. 1), the periphery was described as soft and yellow,

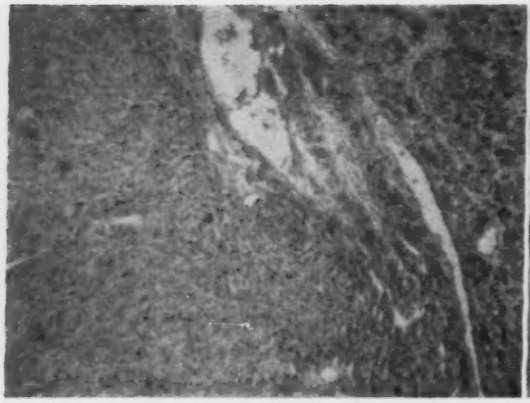

Fig. 1. Low power photomicrograph showing the demarcation between the cortical adenoma (upper right) and the degenerating malignant tissue (lower left).

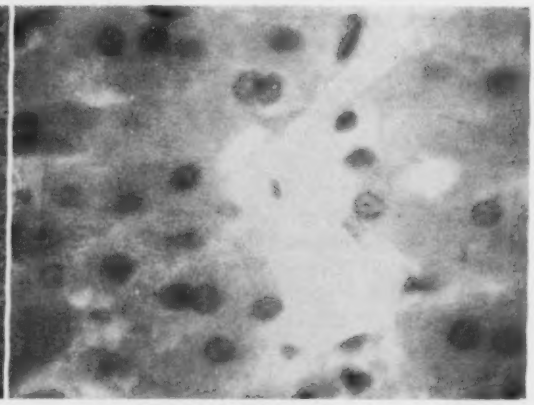

Fig. 2. High power photomicrograph of adenomatous portion of tumor shown in figure 1. Note the regularity of arrangment and a tendency to form glands.

with a central gray area, 7 cm. in diameter, which showed evidence of hemorrhagic degeneration. Another degenerative gray area, 3.5 cm. in diameter, was present near one edge of the mass. Both grossly and microscopically the yellow tissue was consistent with typical adrenal cortical adenoma (fig. 2). On examination of tissue degenerative areas, the cells, although of adrenal origin, were large and irregular in shape, staining characteristics, and arrangement (fig. 3). The line of demarcation between the gray and yellow tissue was sharp for the most part, with a narrow fibrous band between; however, areas suggestive of invasion of the adenoma by the larger irregular cells were seen. The pathologic diagnosis was adrenal cortical adenoma with carcinomatous degeneration.

The patient was given small quantities of steroids postoperatively, because the functional status of the opposite adrenal gland was unknown. The dosage was rapidly reduced and then terminated on the fifth day. On the seventh postoperative day disruption of the wound occurred and secondary closure was necessary. The patient recovered and returned to hard physical labor.

Two years later he began to complain of low back pain, but physical examination and roentgenograms of the spine revealed no abnormality. Four months afterwards, when the back pain had become more intense, x-ray examination revealed sclerotic changes in the fourth lumbar vertebra, with proliferative spurring at the bone margins (fig. 4). The joint spaces were well preserved. The cause of this lesion was unknown, but metastatic carcinoma was considered. The knee jerk was now absent on the right and there was sensory loss involving the fourth lumbar dermatome on the right. A myelogram showed encroachment on the spinal canal in the region of the third to the fifth lumbar vertebrae. Microscopic hematuria was again present; the hemoglobin was 14.5 Gm., the white blood cell count 17,000 with 80 per cent polymorphonuclears, calcium was 9.4 mg. per 100 cc., phosphorus was 2.4 mg. per 100 cc., alkaline phosphatase was 1.8 Bodansky units, and acid phosphatase was 1.3 Bodan-

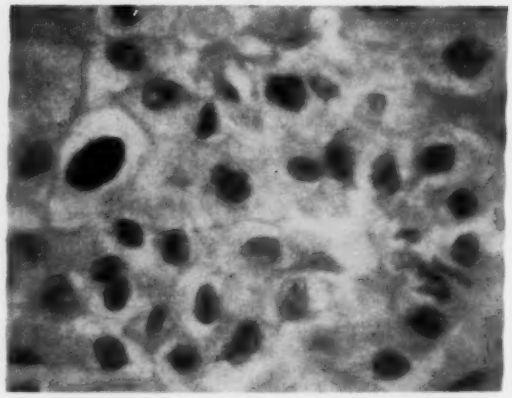

Fig. 3. High power photomicrograph of malignant tissue shown in figure 1. Note irregularity of shape, staining characteristics, and arrangement.

Fig. 4. Roentgenogram of the lumbar spine, showing sclerosis of the fourth lumbar vertebra.

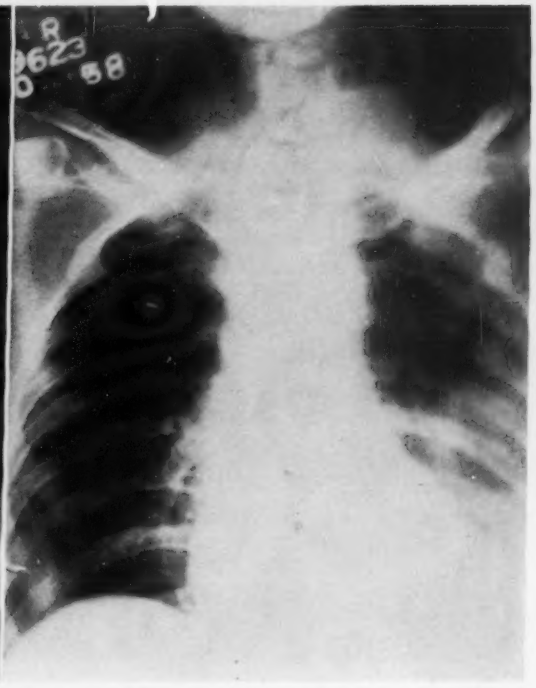

Fig. 5. Chest roentgenogram showing metastasis in the left lower lung field.

sky units. After empirically administered radiation to the sclerotic vertebra afforded no relief of pain, surgical decompression of the fourth and fifth lumbar roots was performed (R. H. Ames, M.D.). At operation the bone appeared abnormally soft, but no definite tumor could be identified. The fifth lumbar nerve on the right was seen to be displaced by a mass of reddish soft tissue overlaid by large blood vessels. Biopsy specimens were described by the pathologist (H. C. Lennon, M.D.) as necrotic tissue, with only a few cells present. It was felt that these cells might be neoplastic, but their origin was in doubt, and they did not resemble adrenal cortical tissue.

The pain was temporarily relieved by the decompression, but recurred three months later, and left cervical cordotomy was performed. Soon after this procedure the pain became generalized on the contralateral side, and opiates were needed in increasing quantity. Sometime during the next several months an irregular abdominal mass was palpated, seemingly fixed to the anterior aspect of the third lumbar vertebra. Concurrently the patient began to complain of pain in the left anterior part of the chest. Another exploration at the fourth lumbar vertebra was performed, and this time a mass of gray tissue arising from the anterior surface of the spinal canal was removed. Microscopically (H. Z. Lund, M.D.) there were atypical round and polyhedral cells. The diagnosis was undifferentiated carcinoma with reactive (probably radiation) fibrosis.

The patient was not made comfortable; he demanded opiates constantly, he had high fever daily, and systemic deterioration became pronounced. The total protein was 6.5 Gm. with 3.2 Gm. of albumin and 3.3 Gm. of globulin. The hemoglobin was now 10.3 Gm., cephalin flocculation was negative, and the alkaline phosphatase was 1.4 Bodansky units. Oral corticosteroid therapy was tried with striking success, and the patient was symptom-free for the next few months (this was three and a half years after removal of the tumor, and a year after the cordotomy). Pain subsequently developed in the left upper part of the chest and the left shoulder, and the irregularly shaped pre-lumbar mass grew larger. Hem-

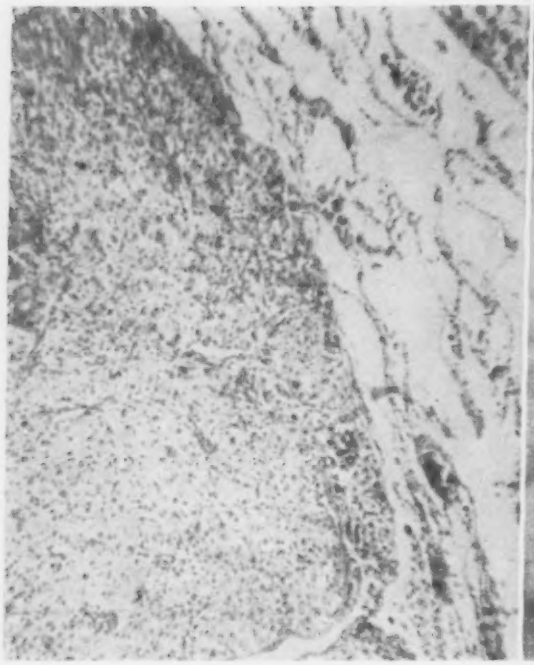

Fig. 6. Low power photomicrograph showing lung metastasis found at autopsy.

Fig. 7. High power photomicrograph of figure 6. Note similiarity to figure 3.

oglobin was 9.6 Gm.; alkaline phosphatase was 5.8 Bodansky units; blood electrolytes, urinary 17 ketosteroids, and 17 hydroxycorticoids were normal. A new sclerotic lesion in the first lumbar vertebra was noted on x-ray, and a few weeks later a lesion projecting into the left pleural cavity from the chest wall was demonstrated (fig. 5).

Marked dehydration, fever, anorexia, and wasting occurred. Terminally paraplegia developed, with paralysis of the bladder and rectum. The patient expired at 49 years of age, eight and one half years after the tumor was first detected, slightly less than four years after its surgical removal and identification, and 18 months after an isolated metastatic lesion in the fourth lumbar vertebra was recognized on x-ray.

At autopsy (J. Harrup, M.D.), metastatic carcinoma was found in the ribs, vertebrae, sacrum, lungs (figs. 6 and 7), liver, and cauda equina, the last by extension from the surrounding bone lesions. Overlying the lower vertebrae and sacrum was a smooth, round, deep purple mass measuring 20x15x12 cm. The right adrenal gland was normal. Generally, the lesions showed extensive necrosis, but there were areas resembling normal adrenal tissue, being yellow and firm on the gross examination and revealing glomerulosa-like arrangement microscopically.

Comment

Adrenal cortical tumors are not infrequently found during routine autopsies. At times it is quite difficult to tell whether there is an actual benign tumor or merely cortical hyperplasia. Usually hyperplastic nodules are small, 1 to 2 cm. in diameter, and have a regular cellular arrangment. The benign tumors tend to be larger, have a definite capsule, present a disorderly architectural pattern, and show individual cellular variation in size, form, and staining characteristics. Likewise, it may be difficult to distinguish a malignant cortical tumor from a benign one. The only absolute signs for diagnosing malignancy, other than the presence of metastases, are invasion of either the capsule or veins. Relative indications of malignancy are necrosis, hemorrhage, calcification, pleomorphism, and atypical nuclei. Some authors[4] believe that benign adenomas may undergo malig-

nant transformation. The tumor of the case being reported showed capsular invasion initially, and it certainly appeared that the malignant area had arisen within by a large benign cortical adenoma. Such an appearance has been typical of the previously reported cases of non-hormonal adrenal cortical carcinoma.

Summary

A case of non-hormonal adrenal cortical carcinoma with osteoblastic metastasis to the fourth lumbar vertebra is described. The tumor was removed four and one half years after it was first discovered; metasases appeared two years later, and death occurred 18 months after that.

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Silo-Filler's Disease

Report of Two Cases in Henderson County, North Carolina

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LESTER B. MCDONALD, M.D.
and
RICHARD A. PORTER, M.D.
HENDERSONVILLE

The following two cases are being reported in order to alert the medical profession to the occurrence of so called "silo-filler's disease" in this state. Curiously enough this rather prevalent agricultural hazard in its various modifications was not clearly recognized and defined by medical investigators until about 1956, at which time reports were first published in the medical literature by several different groups in the middle western states[1].

Report of Cases

Case 1.

A 65 year old white male dairy farmer was seen at his home on October 28, 1956, five days prior to admission, with a history of acute illness marked by severe cough and weakness during the previous two weeks. He dated his illness from the time he climbed an enclosed ladderway to the top of his silo, a distance of 40 feet. This act required about five to eight minutes. The silo was a permanent concrete tower-type structure, and had been rapidly filled with freshly harvested corn silage four days previously. The soil had been heavily fertilized with nitrogen that year and during the preceding several years. The silo and its connecting chute were enclosed and unventilated except for the opening at the bottom of the chute. Half way up the chute the patient began to feel extremely ill and reasoned that he must either climb down or up to the top where he could reach fresh air. He remembered that certain gases prevalent in recently filled silos were heavier than air, so he decided to go up. He reached the top, where he opened a window, put his head out, and revived. He stayed there about 10 minutes and then descended to fresh air as rapidly as possible.

Almost immediately he began to cough and to manifest symptoms similar to previous episodes which he called "asthma." From then on he became very weak, lost his appetite, and took to his bed. The cough became highly productive of thick heavy purulent sputum, but he denied having spit up any bloody sputum during the first week. His wife stated that his appetite had been very poor. He had been content to lie in bed, which was unusual for him. His temperature had been rising to approximately 100-101 F. each night, falling in the early morning hours, accompanied by profuse, drenching sweats. There had been no chest pain and dyspnea had not been pro-

Fig. 1: Roentgenogram made on November 2 1956 at time of admission to hospital. Patient in recumbent position, 50 inch exposure. Marked multiple discrete infiltrative lesions scattered throughout both lung fields, more prominent in the right than the left.

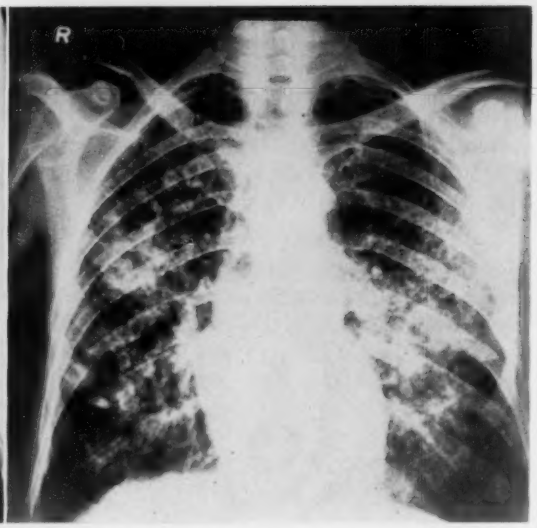

Fig. 2: Re-examination of thorax on 11 November 1956. This and subsequent roentgenograms made in upright position with 72 inch exposure. Marked spotty infiltrative lesions. Little change.

nounced, but he had some shortness of breath after a protracted coughing spell. Beginning on October 28, 1956, he had been treated with intramuscular penicillin, 600,000 units daily for three days, with no improvement, then with oral oxytetracycline, 1.0 Gm. daily for two days; but his temperature was still elevated to 102 F. On the day before admission his sputum was slightly blood-tinged.

Past history: The patient had been a farmer for 10 years but had never had an experience of this type before, although he had heard of men becoming ill in silos. He had his first attack of asthma in 1930, following the plowing of a large area of brush and weeds. He stated that each winter thereafter he had an attack of what he called "influenza," with the development of asthma. He came from Florida to this county in 1946 and thought he had escaped his usual winter illnesses; he rarely had colds, was able to work hard, and was seen by the attending physician in only two episodes of upper respiratory infection in six years (December, 1950, and May, 1952), both responding to three daily injections of penicillin. He stated that he had not seen a physician in the preceding three years, and had had no colds during that time. He had never had pneumonia or pleurisy.

Physical examination: On admission to the hospital on November 2, 1956, the patient was a tall, lean, lanky white male who lay in bed and had every appearance of acute illness. His color was moderately good, and he was not particularly cyanotic. His cheeks were flushed. Respiration was fairly rapid (22 per minute), temperature 102.4 F, pulse 100 beats per minute and regular, and blood pressure 110 systolic, 80 diastolic. The other pertinent physical findings were limited to the lungs: Breath sounds were harsh throughout; vocal resonance and fremitus were not those of consolidation, and there were a few crackling rales mixed with a few large bubbling rales.

Accessory clinical findings: Urinalysis was normal except for a trace of albumin. Blood studies indicated 14.05 Gm. of hemoglobin per 100 cc., and 18,200 leukocytes, per cubic millimeter, with 9 per cent stab cells, 79 per cent segmented polymorphonuclears, 5 per cent lymphocytes, 3 per cent monocytes, 2 per cent basophils, and 2 per cent eosinophils. The sedimentation rate of erythrocytes was 90 mm. in one hour (Westergren method). Three sputum smears for acid fast organisms were nega-

tive. Routine bacteriologic cultures of the sputum were reported as showing staphylococci, streptococci and diphtheroids, and cultures for fungi produced *Candida albicans*. Two cytologic studies of the sputum disclosed no evidence of neoplasm.

On admission a roentgenogram of the thorax (fig. 1) as interpreted by Dr. Karl Kaufman, radiologist, showed marked multiple discrete nodular infiltrative lesions scattered throughout both lung fields, more prominent in the right lung and right base, but also pronounced in the central portion of the left lung field.

Clinical course: Oxytetracycline was given intramuscularly for two days, then oral chloramphenicol therapy was initiated and continued for 15 days. The patient remained acutely ill, with a febrile course characterized by baseline rectal temperature readings of about 101 F. and daily evening spikes to about 103 F., the latter accompanied by free perspiration, lethargy, and at times irrationality. He continued to have severe cough productive of a considerable amount of pink, frothy and mucopurulent sputum. At times the sputum was frankly blood-stained. Harsh breath sounds persisted throughout both lung fields. He felt very weak.

By November 11, 1956, there had been no appreciable improvement in the patient's condition. A chest film at that time (fig. 2) showed little change. On the same date corticosteroid therapy was begun, using 40 units of ACTH intramuscularly per day for three days, and concurrently 5 mg. of prednisone, orally four times daily. The latter was continued in the same dosage about six days, following which 5 mg. was given twice daily for the remainder of his hospital stay and a short time thereafter. The patient's condition improved dramatically within nine hours of the administration of the corticosteroid. He felt much better and his temperature dropped abruptly to normal the same day and remained less than 100 F. rectally thereafter. Nystatin was begun on November 13, and was also continued throughout his hospitalization and for a short time thereafter. While in the hospital he continued to show progressive improvement, although auscultatory findings in the chest persisted in various degrees. He was discharged on November 21, 1956. Several chest roentgenograms showed progressive and complete resolution of the previously described lesions. Two illustrative films are seen in figures 3 and 4 taken on November 14 and December 13, respectively.

Follow-up information is not as precise as might be desired, but the patient apparently continued to have some difficulty with weakness, coughing episodes productive of white mucus, and at times dyspnea, but his weight gradually returned to normal within the next two months. Treatment was conservative, consisting chiefly of standard expectorants.

He returned to Florida to convalesce for about seven weeks during February and March, 1957, and was next seen on April 3, with the same complaints and still had both inspiratory and expiratory musical wheezes in both lung fields. A repeat roentgenogram of the thorax at this time showed complete resolution of the infiltrative and fibrotic lesions in both lung fields, but a slight increase in the small pulmonic markings was still present. Expectorants, bronchodilators, and a regimen of intermittent antibiotic therapy were used over the next several months with variable results, the usual findings on examination being some wheezes in the lung fields. He was last seen professionally on July 30, 1957, at which time his lungs were clear to auscultation. He is still living and working, but a medical report of his present status could not be obtained.

Case 2

A 50 year old white male dairy farmer (who lived only 2 to 3 miles from the patient in case 1) was seen at his home at about 9:30 P.M. on August 6, 1959, with a history of sudden smothering while eating supper a short time earlier. It was learned that he had filled his silo with wet green alfalfa and some clover and pasture grass during the previous day, and after letting it settle overnight had gone back the next evening just before dark for about 20 to 30 minutes to pack it down and level it off a little. This silo was a concrete tower-type structure similar to the one in case 1. In contrast, however, both the silo and chute were open at the top. The silo measured about 35 by 12 feet and held 95 tons of sil-

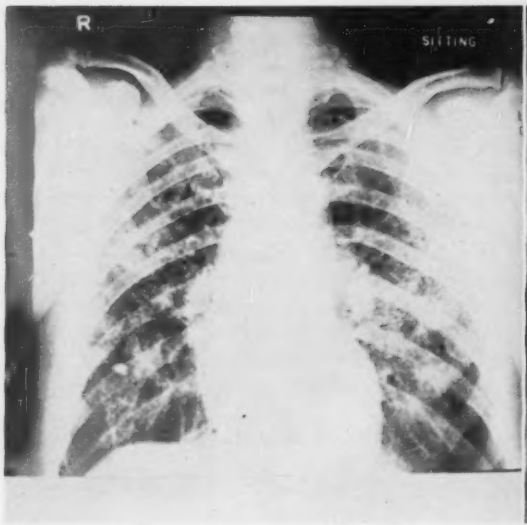

Fig. 3: November 14, 1956. This roentgenogram taken on fourth day of corticosteroid therapy.

Fig. 4: December 13, 1956. Further resolution of previously described lesions. Increase in small pulmonic markings throughout both lung fields.

age as opposed to 40 by 14 feet and a capacity of 125 tons in the first case. About 40 to 50 minutes after leaving the silo the patient noticed difficult breathing which he verbalized as: "Can't get air in . . . smothering . . . short of breath . . . having to breathe hard." He had no previous history of asthma or pulmonary disease except for "pneumonia" in 1930, but recalled having smothering spells, mostly at night, on about six occasions during the preceding month or so, which he attributed to "indigestion or gas." They were relieved by burping, and, unlike the present episode, they did not "close up and shut off" breathing. The dates of these episodes were rather vague, but may have occurred after the first alfalfa ensiling operation around the latter part of April or first part of May, 1959. At that time, however, he did not re-enter the silo for five or six days after the filling.

The patient was a well nourished, well developed male who was sitting up but having progressive intermittent dyspnea with frequent inspiratory gaspings for breath. His color was good, and he did not appear to be in pain. His temperature was 98 F., pulse 100 (strong), respirations 16, and blood pressure 140 systolic, 100 diastolic. Thoracic examination disclosed some wheezes in both lung fields, left more than right, but no dullness to percussion and no change in vocal sounds. The heart was not enlarged, and there was no arrhythmia or murmur. The remainder of the physical examination was not remarkable.

A 12-lead electrocardiogram taken at his home was entirely normal. He was given 100 mg. of Solu-Cortef (hydrocortisone sodium succinate) intravenously, and started on dexamethasone, 0.75 mg. four times daily, given orally at home, the latter being continued in decreasing dosage for a week. No antibiotics were given. He was seen in the office the following morning as directed, and still had some intermittent gasping, but this sympton was less pronounced than on the previous night. Auscultation of his thorax still revealed some wheezing sounds. A roentgenogram of the thorax was obtained at that time and was interpreted by the radiologist as being normal. Seen again three days later as instructed, the patient stated that he still had to take an occasional "deep breath all through the day." On physical examination then his lungs were clear. His symptoms had disappeared by August 14, 1959, and on subsequent examinations in September and October he had remained asyptomatic and his chest was normal on physical examination.

Comment

Several authors[1] have outlined the pertinent features of silo-filler's disease syndrome: Briefly they involve exposure to gas evolved from fresh silage during the initial fermentation stages of ensiling, beginning within a few hours after the start of a silo filling, reaching a maximum between one and two days later, and continuing at a decreasing rate for a week or longer. The irritating gas has been identified as nitrogen dioxide and its dimer nitrogen tetroxide. Several conditions thought to contribute to the high concentration of nitrates in plants under certain circumstances are listed as drought, high-nitrate soils, immaturity of plants, and increased length of photoperiod.

Lowry and Schuman[1b] suggest that there is a continuous spectrum consisting of different types and degrees of bronchopulmonary injury by nitrogen dioxide dependent chiefly upon the amounts of gas inhaled and varying from: (a) acute pulmonary edema with death in less than two days, (b) edema and bronchopneumonia fatal before 10 days, (c) bronchiolitis fibrosa obliterans with death in three to five weeks, (d) bronchiolitis and focal pneumonitis with spontaneous recovery, (e) varying degrees of bronchitis and bronchopneumonia, and (f) chronic pulmonary fibrosis and emphysema.

Case 1 in the present report appears to correlate closely with the criteria for silage gas induced bronchiolitis fibrosa obliterans as outlined by Lowry and Schuman[1b].

Case 2 in this report would appear to fall within the bronchiolitis and focal pneumonitis category.

The use of cortisone in addition to antibiotics and supportive therapy was suggested by Delaney and others[1a]. Lowry and Schuman[1b] mentioned the apparently favorable response to corticosteroids noted in 2 of their 4 cases. They cautioned, however, that the diagnosis of silo-filler's disease must be assured before corticosteroids are used, because widespread infections, particularly miliary tuberculosis, may create a similar x-ray picture (and sometimes a similar clinical picture as well). Grayson's case of acute pulmonary edema[1c] was treated with conventional methods, plus hydrocortisone (Contef) administered intravenously, but the patient failed to respond to the latter and expired 29 hours following exposure to the silage gas, thereby confirming Lowry and Schuman's statement that exposure to the higher concentrations of silo gas or nitrogen dioxide is rapidly fatal in spite of any treatment. Corticosteroids seemed to be very effective in both our cases. It is interesting to note that the previously cited cases of nitrogen dioxide poisoning due to inhalation of fresh silo gas concerned corn silage. Our first case involved corn silage but the second concerned the legumes, alfalfa and clover, together with some pasture grasses. Rather and Harrison[2] state: "The most noteworthy characteristic of legumes is the association with them, in nodules or tubercles growing on roots, of symbiotic bacteria which have the power to fix the free nitrogen from the air into forms that can be utilized by the plant. Because both the seeds and the leaves of legumes are characteristically high in nitrogen, this family of plants has an important place in livestock feeding."

Summary and Conclusions

Two cases which we think conform to the established criteria for particular forms of silo-filler's disease are presented. Both cases involved exposure to fresh silage and illustrate certain results of exposure to varying concentrations of the gas (nitrogen dioxide) in tower silos, and point out the apparently favorable effect of corticosteroid therapy in these instances. They also emphasize the need for the dissemination of more concrete information about the potential dangers to persons engaged in ensiling.

Agricultural methods have been revolutionized in recent years, and an understanding of certain procedures involved may help to explain the possibly increasing incidence of silage gas poisoning. The two dairy farmers in the cases here reported pointed out several enlightening observations to one of us. They stated that formerly in harvesting they would slowly progress through the separate stages of cutting, binding and hauling the crops, and then filling their silos, the total process requiring about a week (depending upon the number of workers and other factors).

Now with the use of mechanical forage cutters and blowers there is rapid harvesting, cutting, and filling of the silo, all phases of which can be accomplished within a single day. They stated that in the last several years they had used heavy nitrogen fertilization on their corn crops. (The commercially available bacteriologically inoculated legumes do not of course customarily require the addition of heavy soil nitrates, since they have the ability to gather free nitrogen from the atmosphere; however, additional phosphorus, in the form of superphosphate, and potassium, in the form of potash, were used.) They concluded that the additional soil nitrogen plus the speed-up in the over-all harvesting and ensiling operation caused more nitrogen to react all at once. In regard to the opinion that the more intensive use of fertilizers may be causing increases in plant nitrogen, a clarifying communication from the fertilizer-research division of the Tennessee Valley Authority[3] is pertinent:

"A brief review by our research staff of literature on plant analysis as affected by fertilization indicates that excessive accumulation of nitrogen in plants is not a common occurrence, although it is known that nitrate buildup may occur under unusually droughty conditions. In general, plants do not take up and utilize more nitrogen than is required to achieve the particular level of dry matter production that is possible under the prevailing climatic and soil conditions. There is generally a high correlation between nitrogen and phosphorus contents of plant tissue, suggesting that each regulates the uptake and utilization of the other."

Precipitation statistics for this area obtained from the United States Department of Commerce Weather Bureau were examined by one of us. Although a formal statistical and scientific analysis of these detailed tables was not performed, they were not interpreted as representing the prevalence of drought conditions during 1956 and 1959. The local county farm agent, Mr. D. W. Bennett, was also consulted for technical advice, with special reference to preventive measures. He stated that for three or four years he had been recommending horizontal rather than tower (upright) silos, pointing out that the latter were much more expensive and no more durable than one of the horizontal variations (trench, bunker, etc.). He felt that well ventilated horizontal silos would be one practical method of dealing with the problem. He stated that since the 1956 case of silage gas poisoning in this county, his staff had been cautioning farmers about going into their silos within the first week after filling.

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Preparations containing more than three ingredients may usually be regarded as therapeutically unsound. Those that may be acceptable are certain analgesic compounds such as acetylsalicylic acid and acetophenetidin, as well as preparations containing the essential vitamins in their recommended dosage. Preparations containing more than vitamins A, D and C, thiamine, riboflavin, niacinamide and perhaps pyridoxine should, however, be looked upon with suspicion, since they are, for most part, of unproved value and expensive; those with two dozens or more ingredients border on the ridiculous. It is time to discontinue such top-heavy polypharmacy. Friend, D. G.: Polypharmacy—Multiple-Ingredient and Shotgun Prescriptions, New England J. Med. 260:1017 (May 14) 1959.

The Role of a Physician in a Changing Society

HUGH A. MATTHEWS, M.D.

CANTON

A good case can be made for Health instead of the Great Jehovah as the god of America. That Health is the prime interest and perhaps the final devotion of the American people is evidenced in many areas. In mass information media—whether press, radio or television—health is constantly among the most popular subjects. The talented author with a doctor story has a good bid for a best seller.

In American industry today management has no choice but to participate in the health field. Labor senses the importance of this god and uses him at the conference table and elsewhere. God Health holds promise of even greater power in this area.

In the agricultural world, God Health is no tottering idol. Thirteen years ago rural America was demanding more consideration for rural health, and was willing to approach the hand of the federal government if no other appeared.

Perhaps the best place of all to discover the relative importance of Health is at the bridge table, in the Woman's Missionary Society, or even the barber shop. In these settings none need be a wallflower. The mere mention of an operation, a new health insurance policy, a new wonder drug, the merits or demerits of a certain doctor, the cancer clinic, or the polio drive puts the informer in the limelight.

Perhaps if the Great Jehovah were sought and found, the solution to America's health problems would be at hand. If enough citizens were seekers, even the process of seeking would likely make Pfizer stock drop precipitously and put Wallace Laboratories out of business. This is not mine to contend. It is mine to accept the situation as it is and analyze the role of the physician in this atmosphere.

At least the minister, priest, or rabbi who wishes to keep his post will be smart to dwell much on health. If he wishes to make the best-seller list or television, he had best dwell on health all the time.

Read before the Section on Practice of Medicine, Medical Society of the State of North Carolina, Asheville, May 6, 1959.
From the Midway Medical Center, Canton, North Carolina.

What in present day America is this goal or god, as the case may be, which is so much desired?

Until about the middle of the nineteenth century, health was considered the mere absence of pain. The physician's role was to give symptomatic relief. He applied leeches, bled, and purged. He applied mustard plasters, ointments, and cupped. The physician was the exclusive dispenser of health, who grew or made his agents for relief.

At the middle of the ninetenth century disease, not symptoms came increasingly to receive the spotlight. Bacteria became known entities. Cause and effect operating in human subjects became the burden of doctors.

Others necessarily became essential to the health program. Bacteriologists pathologists, technicians, even manufacturers, became increasing important. Focus on disease made finding the source of causative agents, and ways and means of prevention, all important. Public health services became essential to the health sciences. In many states, sources of disease were found to be the responsibility of municpal, county, state, and federal governments. In meeting this responsibility, sanitarians, entomologists, sanitary engineers, and other groups became a part of health activity.

Health then became the absence of disease. At the turn of the century, the nation was germ-conscious. Demand was greater, knowledge was greater, and equipment increasingly necessary. Physicians, communities, foundations, and governmental agencies were building hospitals. The nursing profession increased by leaps and bounds. Hospital administration, as a profession, had its birth. Now medical expense involved more than doctors' bills, the pharmacist, the hospital, the nurse, and others had to be paid.

To relieve the financial burden, prepayment medical schemes came into being. Insurance business entered the field of health to stay.

The disease in a man could not be observed until the man was seen. As the twentieth century progressed, medical science was focused not merely on man's symptoms or on his disease, but primarily on man himself. His nutrition, his mental state, his genetic inheritance, and economic and social status were found to be important factors. Scientific clinical medicine now accepts and teaches the concept of the *whole* patient—physical, mental, and social—as the central object of medical practice.

Health has come to mean a state of harmony with one's self. The term "medicine" now implies pyschosomatic medicine.

In the middle of the twentieth century, of which we are a part, God Health is taking on another dimension. Psychosomatic man still stands in the spotlight, but somewhat off center. The light is shifting to the health needs and status of the community.

Dr. Edward G. McGavran, head of the Public Health School of the University of North Carolina, with a profound sense of the sociologic aspects of health, says: "In scientific public health, we no longer treat the individual—the segment of the community—but the total body politic—mental, physical, social and economic."

A revision of the "Principles of Medical Ethics" was adopted by the House of Delegates of the American Medical Association in June, 1957. Section 10 of these Principles reads: "The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual, but also to society where the responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and well-being of the individual and the community."

The present day physician is in a state of change which demands a broadened conception of his role. In every transition in the focus of interest, eminent physicians have rebelled. Change nevertheless took place. History has proved that to ride on the wave of change is folly, to resist change is fatal, but to predict and fashion change is fruitful.

In early America the strongest social unit was the neighborhood. Physiographic conditions, family ties, and other factors brought individuals together. To get what they wanted they evolved social institutions —the school, church, grocery store, and the blacksmith shop. The system geared to its time obtained the objectives desired.

Under the impact of technology neighborhood life is giving away. The most eminent new social system is the town-country community, the type of community in which most of us live. Rural people are moving near the city to work. Urban people are moving out of the city to live, but maintain their jobs in town. Industry is decentralizing by moving to the suburbs and smaller communities. Communities everywhere have industrial development committees.

A revolutionary change is taking place in the public school system. The American people, as one man, are acting on the assumption that a complete community must have a high school, a junior high school, and an elementary school, the entire system operating to serve the given community.

Along with the school are many other community organizations and services. Recreational programs, service clubs, national health foundation chapters, and many special interest groups concern themselves increasingly with health and welfare. Hospital services, water supply, sewage disposal, safety, fire protection, and health clinics are the constant concern of organized groups.

While every man belongs to a community of family, neighborhood, county, state, nation, world, and now possibly of the universe, the community described above is the one coming into focus on the medical scene. Virtually all the people and all the organizations of this community concern themselves with health. The era is at hand when team effort is essential and will be had.

Medical Care— The Physician's Responsibility

The primary role of the physician on the team is medical care. The term "primary" is emphasized and haste made to add that medical care of necessity is his *primary* but not his *exclusive* role. His specific training is to administer medical care, and in this role he is most urgently needed. He will have to remain dedicated primarily to suturing the face that has been cut, treating the diabetes of the obese patient, or controlling the spread of typhoid from

A vine, someone said, is like the human mind - always reaching out for new things to grasp.
PROGRESS...
One way or another people will seek out new ways to cope with old problems. Yet progress must be wisely guided. One doctor says: "The desire of the public to have prepayment medical protection is so urgent that it will buy this protection from whatever plan seems most enticing. Whether you like it or not, prepayment medical care is here to stay. Let us support the system which is voluntary and over which we have adequate control." BLUE SHIELD
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5,000	7,500 to 15,000	75.00 Weekly	114.00	57.50	152.00	76.50
5,000	10,000 to 20,000	100.00 Weekly	150.00	75.50	200.00	100.50
5,000	12,500 to 25,000	125.00 Weekly	186.00	93.50	248.00	124.50
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polluted water. In chronic illness, the majority of physicians will have to expend most of their energy in treating the end results of aging or disease processes.

In answer to the demand for a team approach to health problems, the American physician should be willing to serve as captain of the team, not as a privileged character, but as a servant. He should be willing to bring the team together. From communication will come mutual helpfulness and definition of roles.

The physician should and must become an expert in legitimation. Frequently, all an organization wants from the doctors with respect to a health project is the green light. The green light should be given if the project is worthy of the effort. If the project is not worthy, deserving interest can be redirected to a deserving end far easier than it can bucked.

In this era of change of focus to the newly developing community, the physician needs to interpret his role to the health team. He must help younger members of the team find and define their roles. With the team, through communication and not boycott, he must and can preserve his honored and historic place in health on the march.

The latest *Health Man-power Chart Book* of the United States Department of Health, Education, and Welfare states, "Nearly two million persons are employed in occupations considered in the health field." Among these are dentists, public health nurses, health engineers, health educators, medical and psychiatric case workers, nutritionists, sanitarians, and laboratory technicians. Of the nearly two million health workers, perhaps less than two hundred thousand are practicing physicians.

Even so, if Health is the God of America, the doctor is the priest. All major health organizations and the people of the community want him at the head of the team. If the doctor fails, the health system of this country as it is now known and wanted has failed. The people will make this choice. Interference in physician-patient relationship in certain areas must not be interpreted as a calamity but as a challenge.

The people demand much in health. Two million trained health workers stand ready to help two hundred thousand doctors.

At the recent Lions' Convention in Chicago, a beautiful blind girl with a beautiful voice was soloist. The Minneapolis Lions Club had financed her training at a university and the Juilliard School of Music. When she appeared on the stage, her poise and charm, coupled with the appeal of her blindness, brought the hush of a baptismal service over thousands of men. Soon over the rough faces of America's rugged business men tears began to fall.

The blind soloist sang—"Never Walk Alone."

Dr. Watson S. Rankin

W. C. DAVISON, M.D.
DURHAM

It is a great pleasure for me to be present at the dedication of this new health center. Because the Charlotte and Mecklenburg County Health Department is generally regarded by the United States Government as one of the best in the country, many of my friends from China, Formosa, and other foreign countries have been sent here to study your methods. All of them have been enthusiastic in your praise.

My pleasure is increased by the fact that this building is named for Dr. Watson Smith Rankin, a leading pioneer in health work who has been more than a father to me.

And finally, my cup runneth over because Dr. Hamilton W. McKay, Dr. M. B. Bethel, and Dr. Elizabeth C. Corkey invited me to talk about Dr. Rankin, who is my favorite subject.

Talk made at the dedication of the W. S. Rankin Health Center of Charlotte and Mecklenburg County on Dr. Rankin's eighty-first birthday, January 18, 1960.

From the Department of Pediatrics, Duke University Medical Center, Durham, N. C.

I first heard of Dr. Rankin and his accomplishments in 1916. At that time the public health program of this country needed a strong leader, and Dr. William H. (Popsy) Welch, professor of pathology at the Johns Hopkins since 1883, was chosen by the Rockefeller Foundation to be named professor of public health at the Hopkins. He told me that his only qualification for his new appointment was that two of his pupils had become outstanding in the field of public health—namely, Walter Reed of yellow fever fame, and Dr. Watson S. Rankin, the first full-time state health officer of North Carolina and the best in the nation.

I did not have an opportunity to meet Dr. Rankin until 1926, when the Southern Medical Association met in Atlanta. Since Dr. Rankin knew that I was being considered for the deanship of the Duke Medical School, he and Dr. Paul Anderson slipped into the Section on Pediatrics to hear me talk on the selection of medical students—then, as now, a controversial subject. Since *I* knew that Dr. Rankin was a trustee of the Duke Endowment and would be one of my bosses if I were appointed, I slipped into the Section on Public Health the next day to hear him talk on the needs of rural medicine. That evening Dr. Paul Anderson introduced us, and Dr. Rankin and I formed a two-man mutual admiration society and a father-and-son relationship. For thirty-four years he has been the second "light of my life," a title which Osler gave my wife in 1914.

The printed program for this dedication contains the bare facts of Dr. Rankin's splendid career, which are listed modestly in WHO'S WHO IN AMERICA. He has received many honorary degrees, and has held every office available to leaders in public health, having served as president of the American Public Health Association and of the Association of State and Provincial Health Officers, and chairman of many national and state health committees.

The program, however, cannot begin to record Dr. Rankin's many accomplishments. With the help of my friends, Marshall I. Pickens, F. Ross Porter and F. Vernon Altvater, who also pride themselves on being sons of Dr. Rankin, I have garnered considerable information about these accomplishments and shall mention just a few of them.

In 1905, malaria was such a menace to the citizens of North Carolina that Dr. Rankin went to Panama and climbed all over the canal excavations with Dr. Henry Carter — who, more than General Gorgas and General Goethals, was responsible for the success of the mosquito control program and the eradication of yellow fever in Panama. When Dr. Rankin returned to North Carolina and applied Dr. Carter's methods of mosquito control, the incidence of malaria rapidly declined. After the Panama Canal was finished, Dr. Rankin persuaded Dr. Carter to become the malaria control officer for the Duke Power lakes. None of us would have known of this great contribution to public health if Ross Porter, my wife, and I had not visited Panama with Dr. Rankin three years ago, while on a Duke medical postgraduate cruise, and Dr. Rankin pointed out the landmarks of that earlier visit.

Most of the hospitals in other states are worrying about the stiff standards imposed by the Joint Commission on Accreditation, but in North and South Carolina these standards were gradually and painlessly developed twenty years ago by Dr. Rankin and his staff in the Hospital Section of the Duke Endowment.

Until 1924, many of the hospitals in the Carolinas had been built and maintained by pioneer surgeons who had invested their life earnings in them. Dr. Rankin wisely persuaded the communities, with the help of the Duke Endowment, to buy these hospitals and to maintain them as a community responsibility. As a result of this program and his knowledge of the medical and hospital needs of North and South Carolina, and his plan of community hospitals based on his visit to Dr. Maurice M. Seymour in Canada, the Carolinas have better hospital facilities than most of the other states in the nation.

It is perhaps not generally known that the hospital program of the Duke Endowment, developed by Dr. Rankin, is the model followed by the Hill-Burton bill. Dr. Thomas Parran, then Surgeon General of the United States Public Health Service, and Dr. Vane Hoge, Hospital Director of the United States Public Health Service, toured North Carolina with Dr. Rankin in

1936 and 1937 so that they might study the Duke Endowment program. This program, together with Mr. Duke's emphasis on local responsibility for local hospitals, has been the keystone of the Hill-Burton program.

Rising hospital costs (ours at Duke went from $3.81 per patient day in 1933 to $24.55 at present) would have bankrupted hospitals all over the country if it had not been for the Blue Cross program, which Dr. Rankin fathered by helping to develop Dr. Tom W. M. Long's pioneer plan in Roanoke Rapids of a weekly pay deduction of twenty-five cents per employee for hospitalization. With the help of Dr. Rankin and the Duke Endowment, this plan grew into the Hospital Care and Hospital Saving Associations, which are models for Blue Cross plans in other states.

Dr. Rankin's interest in medical education has been of inestimable help to the Duke University Medical Center, as well as to medical schools everywhere. In 1926 a former president of the American Medical Association advocated the establishment of a series of second-rate medical schools throughout the country, whose graduates would not know enough medicine to practice in the cities. Dr. Rankin promptly invited him to tour North and South Carolina, in order to show him that good medical care is just as necessary for rural areas as for cities, and that it was being provided with the aid of community hospitals which attracted keen medical graduates to small towns.

Dr. Rankin also is responsible for the youthfulness of the original Duke medical faculty. He and I had both learned from Osler that a keen young man would make a better medical teacher than one who was more mature and who might be inclined to rest on his laurels; consequently, whenever we had a choice of candidates, the younger man was selected. As a result, the average age of the original Duke medical faculty was 34 years—the same as that of the original Hopkins faculty. Dr. Rankin himself is the best example of youth—he was only 24 years of age when Dr. Welch recommended him for the professorship of pathology at Wake Forest, 26 when he became dean of the Wake Forest Medical School, and 30 when he was made North Carolina's first full-time health officer.

One more anecdote: Dr. Rankin's career in public health was launched by the hookworm. While in Baltimore, he performed one of the first autopsies in this disease and later at Wake Forest he found it in many patients. As a result, he became so much interested in preventive medicine that Dr. R. H. Lewis, chairman of the North Carolina State Board of Health, was able to persuade Dr. Rankin in 1909 to become one of the first full-time state health officers in the United States.

Incidentally, I also received my appointment by way of the hookworm. In 1925, after Mr. James B. Duke died, Dr. William P. Few, president of Trinity College (later Duke University), was faced with the problem of starting a medical school. Fortunately for me he knew Dr. Wickliffe Rose, who was in charge of the hookworm campaign in North Carolina, which Dr. Rankin had started. Dr. Rose referred Dr. Few to Dr. Welch, who persuaded Dr. Few to appoint me as dean, thereby completing the life cycle of the hookworm—now a forgotten disease.

Hookworm and malaria will pass into oblivion — thanks largely to Dr. Rankin's efforts—but this new W. S. Rankin Health Center will remain as a monument to the man who has done so much to improve the health of the citizens of North and South Carolina. The dedication of this building is a fitting tribute to him on his eighty-first birthday.

Last but not least. Dr. Rankin started as a Presbyterian, became a Baptist, now works for the Methodists, and everyone loves him.

North Carolina Medical Journal

Owned and published by
The Medical Society of the State of North Carolina,
under the direction of its Editorial Board.

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NORTH CAROLINA MEDICAL JOURNAL

300 South Hawthorne Road, Winston-Salem 7, N. C. Questions relating to subscription rates, advertising, ect., should be addressed to the Business Manager, 203 Capital Club Building, Raleigh, N. C. All advertisements are accepted subject to the approval of a screening committee of the State Journal Advertising Bureau, 510 North Dearborn Street, Chicago 10, Illinois, and/or by a Committee of the Editorial Board of the North Carolina Medical Journal in respect to strictly local advertising accepted for appearance in the North Carolina Medical Journal.

Annual subscription, $5.00 Single copies, 75c

Publication office: Carmichael Printing Co., 1309 Hawthorne Road, S.W., Winston-Salem 1, N. C.

FEBRUARY, 1960

COUNTY MEDICAL SOCIETY OFFICERS' CONFERENCE

The first annual conference of County Medical Society Officers, held in the Carolina Hotel at Pinehurst on Saturday, January 30, was appropriately entitled "Navigating the Medical Waters." Rain began the night before and continued steadily until the next day. In spite of the weather, however, there was a good attendance, and the enthusiasm of the men present was not dampened. The wives, however, were quite disappointed in being shut in for the week end.

Thanks to the chairman, Dr. E. T. Beddingfield, the Conference was run on schedule and closed promptly at 4 o'clock.

Perhaps the high light of the program was a comparison of the American and the British system of medical care by Dr. John C. Duke. Dr. Reckless, who has practiced under both systems, gave an illuminating discussion which was appreciated by all. While he gave the pros and cons of both, he left no doubt as to his preference for the American system.

Dr. Donald Koonce gave excellent advice on the "Modus Operandi of County Societies." Dr. Wayne J. Benton spoke on finances and explained the way in which the Society's income is received and how it is spent.

Mr. C. A. McKnight, editor of the *Charlotte Observer*, gave "A Non-Medical View of the Profession"—an excellent opportunity to see ourselves as others see us.

Dr. Leonard Martin (Ph.D.), assistant director of the Economic Research Department, American Medical Association, gave an analysis of the cost of medical care in which he showed that the doctors' share of money spent for medical care is much smaller than is generally believed.

In the panel discussion of insurance more questions were raised than were answered, but at least the conference members gave it close attention. Among the questions raised was whether or not the cancellation of so many policies by some companies is justified; why some companies reject the standard forms prepared by our Society; and how to determine the validity of claims for diagnostic surveys. Insurance for the home-care of patients when authorized by the physicians was advocated. Mr. Charles Gold, State Commissioner of Insurance, was asked how many riders should be attached to a policy for holders past 65. His reply was, "not more than one."

The question as to whether patients abused hospital insurance was given a sort of "yes and no" answer. A good many thought that insurance companies would save money by paying for some diagnostic procedures, especially x-rays, without requiring the patient's admission to the hospital.

"Successful Local Projects" of seven counties proved to be most interesting and stimulating. The projects discussed were: "Medical-Legal Cooperation in Forsyth County," Julius A. Howell, M. D.; "Medical Press Relations in Wilson County," William G. Spencer, M. D.; "Health Fairs and Scholarships, A Community Project in Haywood County," Hugh A. Matthews, M. D; "A Welcome Wagon Letter to New

Residents," W. J. Senter, M. D.; "Cooperation with the Welfare Department in Harnett County," Bruce B. Blackmon, M. D.; "Science Fair Sponsorship in Mecklenburg County," James P. Alexander, M. D.; "Cabarrus County Projects, Tetanus Program and Uterine Cytology Survey," M. S. Tuttle, M. D.

The final message from President John Reece is to be published in the NORTH CAROLINA MEDICAL JOURNAL and will well repay reading, even to those who heard it.

A movie, "On Call to a Nation," BBC Documentary Report on the British Medical System, was scheduled for 7:30 P.M. but did not get under way until after 9 o'clock. Only a comparatively few saw it, but those who did agreed that it confirmed the viewpoint of Dr. Reckless.

The verbal comments on the Conference were generally favorable. Its effects will be far-reaching if the county officers present will take back home with them the information and inspiration offered by the program participants.

* * *

Guest Editorial

PLANS FOR MORTALITY STUDIES IN 1960

Most of us have been eye witnesses to the scientific revolution taking place in the twentieth century. We have seen the wide use of automobiles, the automation of industry, the mechanization of the household, and, in medicine, the introduction of antibiotics, new chemotherapeutic agents, and new techniques in diagnosis and surgery. Mortality statistics recorded for the first half of the century show clearly the effects of medical advances on improvements in health. But we know nothing of the effects on longevity of differential changes in standards of living, or of our new way of life. More than one hundred years after Dr. William Farr pointed out the relation between levels of living and mortality, the vital statisticians in the United States have not achieved a satisfactory measure of mortality for the socioeconomic groups of our population.

The information on the death certificate can be and has been used to determine death rates by cause of death, age, sex, marital status, and, for persons of work experience, by broad occupational groups. But there is no information on the death certificate that enables us to relate the mortality of women and children to the occupation of the husband or father, or to relate the mortality of any group of education, income, housing, size of family, and other important socioeconomic variables.

The most comprehensive source of socioeconomic information about each person and his family is the decennial Census of Population in which, for 1960, about 180 million persons in 54 million households will be enumerated. A proposal has been made for a new type of mortality study that would utilize the information collected in the April 1960 Census. For a selected period after the enumeration date, the census records of persons who were alive at the time of the census but who died in the months immediately following will be located. The information on the census record will be correlated with the information on the death certificate. This matching procedure will expand tremendously the number of variables that can be related to the cause of death reported by the physician on the death certificate.

The key to the linking of the death record and the census record is the address of the decedent. The census records are filed according to the enumeration district (the area of a city or county assigned to one enumerator) in which the family lived. The enumeration district in which the "usual residence" of the decedent given on the death certificate is located can be identified. Then this enumeration district file will be searched for his address, his family and the individual. When the decedent is located, the statistical information from both records can be brought together mechanically. It is important to note that this procedure preserves the confidential nature of the census record and of the death certificate. The additional information that could be obtained by matching the 1960 death and census records enhances the value of that basic demographic document, the death certificate. These data may establish the beginnings of a new series of rates reflecting the effects of our twentieth century way of life.

J. W. R. NORTON, M.D.

CURED CANCER CONGRESS

At a meeting of professional men a highly intelligent lawyer said that he had never known a person who had been cured of cancer. The man sitting next to him immediately said: "Well, you see one now. Look at this scar on my face, which marks the spot where one was removed many years ago."

It is unfortunate that so many people share the view of the lawyer and so few patients freely admit that they have ever had cancer.

One of the most constructive moves made by the American Cancer Society is to sponsor a number of cured cancer congresses, with patients who have been cured selected to represent a variety of cancer types.

The first such congress for North Carolina is to be held in Raleigh at 7:00 P.M., March 26, at the Sir Walter Hotel. Letters have been sent to all presidents of county medical societies, to chairmen of county society cancer committees, and to the medical advisers of several county units of the American Cancer Society. These men were asked to select patients who have had no recurrence of cancer for at least five years, and who were willing to attend the state congress as living, tangible evidence that cancer can be cured. From the case reports submitted will be chosen as wide a variety of cancer types as possible.

It is hoped and expected that the publicity given this congress will do much to dispel the unwarranted fear and ignorance of cancer that is so widespread.

* * *

WHICH PATH TO MEDICAL SECURITY?

It is now 20 years since the medical profession gave birth to prepaid medical care, but its ultimate patterns of operation and control are yet to be determined.

While most of us recognize that the public will make the eventual decision, nevertheless we doctors have it within our power —if we will—mightily to influence that decision. For the simple fact is that, in the long run, the people—our patients—will support that system of medical care prepayment which offers them the best assurance of satisfactory professional service through physicians and institutions of their own choosing.

Today, several contrasting programs of medical prepayment are competing for popular and professional favor—each embodying a distinct concept of the relationship between patient and doctor.

One such program is the limited cash reimbursement program of the insurance industry, which offers the insured certain dollar indemnities against certain medical contingencies, irrespective of the physician's charges for the service required.

Another major program is medicine's Blue Shield Plan, which seeks—through professionally negotiated schedules of payment and, in most areas, through the agreement of participating physicians—to assure the patient of fully paid professional services.

A third program is the "closed panel" of physicians. Operating frequently under labor or other lay auspices, this plan undertakes to provide a comprehensive service through a selected group of physicians remunerated by salary or per capita allowances, regardless of the volume of service required of them.

Which of these programs most faithfully reflects the traditional pattern of American medical practice? Which program is most clearly motivated—as medicine itself is motivated—to render service to the patient and to meet the needs of all segments of the community? Which program returns the fullest value to the patient and most fairly compensates the doctor? Which program best utilizes and protects the modes and ideals of practice that have earned us the envy of others?

* * *

SILO FILLER'S DISEASE

The paper on Silo Filler's Disease in this issue, by Dr. Evans, McDonald and Porter, deserves special mention. It calls attention to a comparatively recent occupational hazard of farming. The authors have given a vivid description of two types of the disease. They had the clinical acumen to profit by their experience with the first case and recognize and treat promptly their second one. Evidently they have been helped by keeping up with the current medical literature.

Such case reports are valuable. The editorial board of the NORTH CAROLINA MEDICAL JOURNAL is glad to accept such worth while contributions as this one.

Clinicopathologic Conference

Forsyth County Heart Symposium, Winston-Salem, October 9, 1959

MONROE T. GILMOUR, M.D.
CHARLOTTE
and
ROBERT W. PRICHARD, M.D.
WINSTON-SALEM

IDIOPATHIC MYOCARDITIS

Clinical history: The patient, a 41 year old white man, was in relatively good health until three and a half years before admission, when he began to have cough and exertional dyspnea. These symptoms progressed for six months. At this time he first consulted a physician, who treated him with antibiotics for a respiratory infection, with slight improvement. Shortly thereafter congestive heart failure, with mild dyspnea and slight enlargement of the liver developed. The heart was enlarged to percussion and on fluoroscopy. The blood pressure was 120 systolic, 90 diastolic, and the pulse was 126 and regular. An internist was consulted, and gave a diagnosis of probable silent myocardial infarction. The patient improved on a regimen of diuretics, digitalis, and rest. During the next year his heart continued to enlarge, although the symptoms remained under control and he was able to do light work. Until the final admission he intermittently manifested various signs of failure, largely consisting of basal rales and slight ankle edema. His heart continued to enlarge, and about two months before the final admission the dyspnea increased and he had a systolic gallop rhythm, a severe cough, and increasing orthopnea and insomnia.

Immediately before his admission to the North Carolina Baptist Hospital he was a patient in another hospital, where his pulse was found to be 120 and regular, with a "definite diastolic gallop rhythm." He was treated for congestive heart failure and improved markedly, losing 14 pounds of weight during the first hospital week. After the first few hours his temperature was normal throughout his hospital course. Then left-sided hemiparesis and coma suddenly developed and he was referred to the North Carolina Baptist Hospital.

Physical examination: The patient was an unconscious white man who could move his right side but had complete paralysis on the left; he responded occasionally to loud stimuli. The temperature was 100, pulse 110, respirations 24, and blood pressure 120 systolic, 84 diastolic. The pupils were equal and regular, and reacted to accomodation and stimuli. The fundi showed slight venous engorgement. His neck was rigid. His chest expanded poorly. The heart was enlarged 2 cm. lateral to the mid-clavicular line in the fifth interspace. There was diastolic gallop rhythm at the apex, with no murmurs. The abdomen was soft, giving evidence of recent weight loss. There was no peripheral edema.

Accessory clinical findings: The urine was normal. The hemoglobin was 15 Gm., sedimentation rate 10 mm. per hour, platelets were adequate, the white blood cell count was 8,300, with a normal differential. The white cell count rose to 17,000 on the third hospital day. The blood urea nitrogen was 22 mg. per 100 cc., and the total serum proteins were 7.2 Gm., with a normal albumin-globulin ratio. The carbon dioxide combining power was 15.7 mEq. per liter, chlorides were 98.4 mEq. per liter and sodium was 136 mEq. per liter. A second blood urea nitrogen determination done the following day was 32 mg. per 100 cc. The coagulation time was 10 minutes, and the prothrombin time was normal.

A lumbar puncture was done, revealing a normal pressure of 110 mm.; protein, 58 mg. per 100 cc.; sugar, 92 mg. per 100 cc.; and a total cell count of 11, with 10 red cells. Fluid was grossly clear. An electrocardiogram showed sinus tachycardia with rare premature beats, first degree atrioventricular heart block, and left axis deviation.

Hospital course: On the second hospital day the patient responded slightly to stimuli and said a few words. Digitoxin and Diuril were continued. He became progressively more febrile, the temperature rising to 105 F. on the fifth hospital day. Measures to lower the temperature were ineffective, and the patient died quietly. Terminally there were Cheyne-Stokes respirations and marked tachycardia.

Clinical Discussion

DR. GILMOUR: I must say that our patient has been allowed to say very little for himself. One would get the impression that his Boswell, in presenting this case,

was more concerned with a laboratory specimen than with the articulate, puzzled, and progressively sicker human being we are considering this afternoon. For this patient went from good health to chronic illness to death in an amazingly uncomplaining fashion, a fact which may itself be significant.

At 38 years of age we see him first, relatively young and always healthy, with no history of significant illness. We see him becoming troubled by a cough and slight shortness of breath on exertion, which is not severe enough even to cause him to consult a physician for six months. When he does consult a physician, one of the miracle drugs works no miracle, and because his improvement is only slight and not sustained, he again seeks medical advice. On this occasion, after a somewhat more exhaustive study, another type of treatment is instituted, and seems to help. In order to do even light work, however, he finds it necessary for the next two years to remain under medical supervision and to rest a great deal. All in all he had to take care of himself so carefully that it must have become increasingly apparent to him, as he noted recurrent cough, poor wind, and occasionally some swelling of his ankles, that whatever the illness was, it was far from cured.

Two months before his final hospital admission all these symptoms became aggravated to such a degree that he was unable to sleep—a situation which led at last to his admission to a hospital. Here he was greatly encouraged by his progress. He lost 14 pounds of weight in one week and was able to breath a great deal better. Then, just as he seemed to be improving, the lights went out and he can tell us no more.

His physicians, however, take up the story, describing how, when first seen three years ago, he seemed to have simply a respiratory infection. This did not respond to antibiotics as it should have responded, and soon it became increasingly apparent that he was in what appeared to be congestive heart failure, with a blood pressure of 120 systolic, 90 diastolic, pulse 126 and regular, moderate enlargement of the heart to percussion and on fluoroscopy, and slight enlargement of the liver. As an explanation for these findings and for the heart failure, a consulting internist suggested "a silent myocardial infarction."

Routine treatment for the failing heart, including rest, digitalis and diuretics, resulted in some improvement and enabled the patient to do light work over the next two years, but apparently only under medical supervision. Even then during the second year he had occasional relapses during which basal rales and ankle edema reappeared. During all this time there was progressive enlargement of the heart, and two months before his death a gallop rhythm, described as systolic, was first heard.

Two months later, in spite of treatment, he was so much worse that he was admitted to a hospital, apparently for the first time. His pulse was found to be 120 and regular, and a definite diastolic gallop rhythm was now described. Except for a slight elevation of temperature a few hours after admission, he was afebrile during a hospital course of one week. He improved greatly and, having lost 14 pounds, seemed better, when left hemiparesis and coma suddenly developed, and he was transferred to North Carolina Baptist Hospital.

Here he was found to be unconscious, responding only slightly to strong stimuli. The temperature was normal (100 F., probably rectal), respirations 24, blood pressure 120 systolic, 80 diastolic. On physical examination, recorded in the protocol, the heart was found to be enlarged 2 cm. lateral to the mid-clavicular line in the fifth interspace. A diastolic gallop rhythm was heard at the apex, but there were no murmurs. The liver and spleen are not mentioned. There was no peripheral edema, and nothing is said about the presence or absence of sacral edema.

On the second day it was thought for a time that he was a little better; he seemed to respond to slighter stimuli and even tried to say a few words. But then he became progressively febrile and worse, until his fever reached 105 F. on the fifth day and he died quietly with Cheyne-Stokes respiration and marked tachycardia.

Accessory laboratory data are relatively meagre. Early in his illness, fluoroscopy is reported to have shown cardiac enlargement. If other roentgen studies were done, they are not mentioned. All other laboratory data are those of his last hospital admission.

Urinalysis and blood counts were normal, with a later rise in the white cell count to 17,000 on the third day as the patient's temperature began to rise. The blood urea nitrogen was 22 and later 32 mg. per 100 cc. The total protein count was 7.2 Gm., with a normal albumin-globulin ratio. Chlorides, sodium and the carbon dioxide combining power were essentially normal, with possibly a slight acidosis. Potassium is not mentioned. Prothrombin and coagulation times were normal. The spinal fluid was clear and under normal pressure. The spinal fluid protein was 58 (possibly slightly elevated), sugar, 99; and the cell count was 11, including 10 red cells. Crenation is not mentioned.

Electrocardiograms are reported as showing sinus tachycardia and an occasional premature ventricular contraction, first degree heart block, with a slightly prolonged P-R interval and left axis deviation. Other findings which might be mentioned are a QRS amplitude of the limb leads within the lower limits of normal, a QRS interval at the upper limit of normal, deep Q waves and deep S4, and high R 5-6—findings which might be compatible with left ventricular hypertrophy, early intraventricular block, and myocardial damage, particularly in the region of the septum and conduction system.

Thus we see a man who, with no previous illness, manifested signs compatible with congestive heart failure associated with an enlarged heart without murmurs. In spite of treatment these symptoms progress inexorably, with increasing heart failure and cardiac enlargement, over the course of three and a half years, until admission to a hospital becomes necessary. During his hospital course left-sided hemiplegia suddenly develops, and after five or six days, he dies with high fever, Cheyne-Stokes respiration, and tachycardia.

During all this time, until the terminal phase, no mention is made of pain, cyanosis, significant fever, weight loss, or other evidence of illness, save that relating to his heart and what is apparently heart failure.

What could cause such a chain of events? Although this is a heart symposium, let us first consider extracardiac illness which might conceivably result in this picture, considering, first, metabolic and, second, pulmonary disease.

Among the general metabolic illnesses are some which I shall mention briefly only to discard.

Primary systemic amyloidosis is associated with cardiac involvement in 80 per cent of the cases, with congestive heart failure in 50 per cent and death from heart failure in 40 per cent of the cases. Nonspecific electrocardiographic changes, low voltage T wave changes and conduction defects may be present, and cardiac enlargement may be noted. These changes, however, are usually associated with other signs of amyloid disease throughout the body—lymph node involvement, and so forth—and the cardiac enlargement is not apt to be as great nor as progressive as in our case.

Secondary amyloidosis is associated with evidence of chronic disease or infection, and usually with albuminuria. Since primary cardiac amyloidosis is localized in the heart and usually occurs in people of advanced age—almost always over 70—I think this diagnosis may be discarded.

Glycogenosis of the heart is a disease of infants who rarely survive the first year of life. Rarely glycogen disease in adults occurs as a vague entity, but there is nothing in this case to suggest it. Lipochondrodystrophy, or gargoylism, is associated with dwarfism accompanied by many other deformities, together with valvular involvement and a failure to survive long after early youth. Hemochromatosis is usually associated with bronze diabetes, multiple transfusions or some other metabolic disorder and with other evidence of liver disease. Sarcoidosis need not, I think, be seriously considered, nor lupus, scleroderma, sickle cell anemia, so-called adiposity of the heart, and other rare conditions at times associated with cardiomegaly.

Beri-beri heart disease should be mentioned. There is no history of alcoholism or malnutrition in this patient, and no indication of improvement on a controlled diet. There are no signs of peripheral neuritis or pellagra, as the patient's blood count and total protein were normal. Neither is there evidence of the high output type of failure, of peripheral vasodilation with increased pulse pressure, or of accumulation of fluids in other serous cavities such as might suggest beri-beri.

Thyroid heart disease should always be considered in unexplained heart failure. This condition, like beri-beri and other types of curable heart disease, is one that we should always try to recognize, since cure is to be preferred to management, particularly in heart disease.

Thyroid heart disease can also be mentioned only to be discarded in this instance, however. Except for tachycardia, noted each of the few times the heart rate is mentioned (and these during episodes of failure), there is really no characteristic sign of hyperthyroidism in this patient or in his heart. Auricular fibrillation, often associated with hyperthyroidism, did not develop. Hypothyroidism amounting to myxedema may result in cardiac enlargement, low QRS complexes (usually even lower than in our patient), and in heart failure; but again there is no evidence even suggestive of myxedema. I shall not labor this point further, just as I shall not expand on the heart failure associated with secondary cardiac enlargement, sometimes seen in Paget's osteitis, cirrhosis of the liver, atrioventricular fistula, and other conditions.

Aside from these metabolic possibilities, we should mention the fact that chronic pulmonary disease such as emphysema or the generalized pulmonary infiltration that occurs in silicosis, berylliosis, some chronic infectious diseases of the lung, or diffuse infiltration of the lung by certain types of pulmonary tumors might result in secondary cardiac hypertrophy and failure. In such instances, however, there should be evidence of cor pulmonale with right axis deviation, and there should be more evidence of the primary lung disease than this patient presents.

Similarly, one should never forget the possibility of chronic, recurrent multiple pulmonary embolism as a cause of what appears to be heart disease and heart failure. Again, in this patient there is no evidence of right-sided heart strain, either chronic or acute, and there are no past symptoms which would lead one to suspect pulmonary emboli or a source of chronic pulmonary embolism either in the heart or periphery. Consequently, this diagnosis, too, must be discarded. And so I must conclude that the primary illness in this patient is neither a generalized metabolic disease nor a chronic pulmonary disease.

But now let us turn to the heart itself and try to discover why, in a healthy and relatively young man, this vital organ should have become enlarged and in the process should have produced a train of symptoms over three and one-half years which we must accept, as they are described in this protocol, as evidence of an inefficient, failing myocardium, with resulting congestive failure.

Could disease of the pericardium cause this picture? Indeed, disease of the pericardium can cause heart failure, but I doubt if it did so here. Constrictive pericarditis results usually, though not always, in a small quiet heart; and there are other characteristics which rule it out here. Certain types of adhesive pericarditis that do not produce generalized constriction may result in enlargement of certain cardiac chambers, depending on the in-flow or the out-flow tract or other area involved by the adhesions. But such general cardiac enlargement as this apparently was, and the clinical course which this case followed, would be unlikely.

Inflammation of the pericardium, effusions within the pericardium, tumors of the pericardium—none are really suggested here.

I do recall one case of apparently progressive cardiac enlargement over many years which eventually proved to be due to a large, diffuse benign tumor (as I recall, a lipoma) of the pericardium, but its course was relatively benign and I believe that it did not adversely affect cardiac function to any great degree.

Congenital heart disease is mentioned only to say that there is nothing to suggest it as a background for the development of the clinical picture seen in this patient at his age.

Valvular heart disease, when so far as we know no cardiac murmurs were heard at any time over a period of three years, must be dismissed for lack of evidence, though occasionally unsuspected valvular lesions are discovered in a heart where murmurs were thought to be absent or insignificant. Nor can subacute bacterial endocarditis be seriously entertained as a diagnosis in the absence of murmurs.

Infectious processes may involve the heart and result in so-called myocarditis and eventually in cardiac hypertrophy, dilatation, or both, with failure. But there is no evidence that present or past infection played a primary role in this case, and such a diagnosis would have to be made on microscopic rather than clinical grounds.

In this connection, it is well to note that the patient's serologic status, either for his blood or for his spinal fluid, is not reported in the abstract. We will recall that aneurysms of the ventricles occasionally give a false appearance of cardiac enlargement. Such aneurysms, however, usually are the result of previous myocardial infarction and are not, like aneurysms of the aorta, the result of syphilitic infection or of medial sclerosis.

Coronary heart disease is one of the chief causes of cardiac enlargement and heart failure, though the enlargement is more apt to be pronounced when associated with hypertension, which this patient apparently never had. It is to be recalled that an early consultant made a diagnosis of "a silent myocardial infarction," probably basing his conclusions on the electrocardiographic changes we already have described, plus the fact that *something* had apparently happened to this patient's heart. I believe that so-called "silent" coronary occlusions are the result of inattention on the part of some patients to their symptoms or of their inability to describe these symptoms accurately, or possibly of inattention on the part of doctors to details of the history. I cannot accept a diagnosis of coronary heart disease as the basis of progressive cardiac enlargement and failure over the course of several years without the patient's having at any time experienced subjective evidence of coronary insufficiency as manifested by angina of exertion or emotion, or by a recognizable episode of more severe ischemia or infarction.

Tumors, both metastatic and primary, malignant and benign, do indeed affect the heart and pericardium or any part of either, and may at times give rise to conduction defects, cardiac enlargement and failure, and other changes. Tumors within the heart usually are myxomas, and may simulate valvular disease and lead to cardiac enlargement. There are usually murmurs which change with position and possess other characteristics that make the diagnosis possible, particularly by visualization of the cardiac chambers. Lipomas, rhabdomyomas, sarcomas, endotheliomas, hemangiomas, and lymphoendotheliomas may affect various parts of the heart and conduction system but are unlikely to cause generalized enlargement. A primary malignant tumor of the heart itself is rare indeed. Three hundred cases are reported in the literature, and of these only 13 were diagnosed *ante mortem*. Nor is there anything here which would enable me to make a diagnosis of the fourteenth.

By now it would seem that we had exhausted all the probabilities without arriving at a diagnosis. We have not, however, except indirectly in mentioning tumors, myocarditis, metabolic disease and the like, considered the primary disease of the myocardium and endocardium itself as the cause of this syndrome.

There is a condition reported in this country as idiopathic cardiac hypertrophy which warrants our consideration. It was first reported in the French literature in 1901. Spodick and others, in 1958, found 72 acceptable cases in subsequent medical literature and added 8 cases of their own. The etiology of this group of cases is obscure, as the name would indicate. A background of nutritional deficiency is suggested because of certain similarities to the endocardial fibroelastosis reported as occurring on a deficiency basis in various groups of African natives, but this is only a hypothetical relationship. Similarly, fibroelastosis has been reported in infants and children, apparently on a congenital basis, possibly with a background of anoxia. It has also been described in adults.

This syndrome, as it is seen in adults, may prove to be simply a syndrome rather than a disease entity, as any idiopathic syndrome may prove to be. It usually occurs in the fourth and fifth decades, and is seen in both the Negro and white races, usually in men, usually laborers. The outstanding clinical features include progressive, intractable cardiac enlargement and failure, often with embolization, running a course of a month to years. Evidence of other disease usually is lacking, as is evidence of infection. Gallop rhythms, probably simply indicative of myocardial weak-

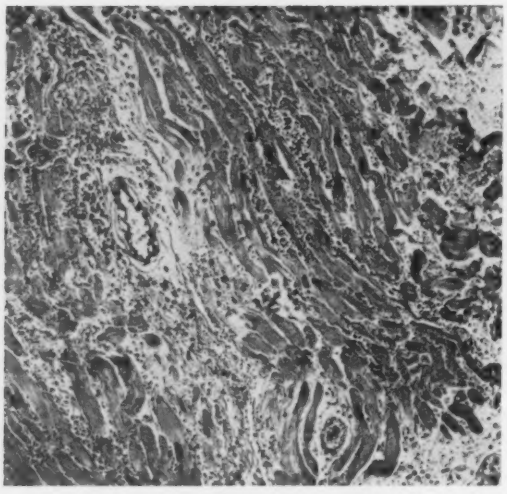


Figure 1

ness, are frequent, and are associated with signs of cardiac failure.

Electrocardiographic changes are nonspecific, with bundle branch block, prolongation of P-R interval, ST depression and T wave inversion, particularly in the lateral V leads, as was described in this case. The diagnosis must, to a large degree, be made by exclusion, as ours has had to be.

This, then, is my conclusion and my diagnosis: idiopathic cardiac hypertrophy with *endomyocardial* fibrosis. I would predict the following pathologic findings: first, in the brain an area of softening in the right hemisphere secondary to an embolus; second, in the lungs terminal broncho-pneumonia and probably small emboli as an incidental finding but possibly contributing to some of the episodes of recurrent failure. In addition, there should be severe passive congestion secondary to heart failure and probably terminal bilateral pleural effusion.

In the heart, I would expect hypertrophy to predominate over dilatation and to involve the left ventricle more than the right, and I would expect the heart to weigh between 550 and 650 Gm. The coronary vessels I would expect to be normal, as would be the valves and the pericardium. The endocardium should be the site of mural thrombi localized over areas of thickening and of fibrosis.

The myocardium I would expect to find rather firm but with an occasional hemorrhagic area. Microscopically, there should be hypertrophy and degeneration and connective tissue proliferation, with numerous areas of interstitial and perivascular fibrosis, most marked in the endocardium and subendocardial layers, and possibly most marked, in this case, in the left ventricle and in the septum, involving the conduction system. There would probably be only small loci of secondary cellular reaction, without any evidence of a marked or active myocarditis. There might also be a thickened fibroelastic layer at the base of the endocardium. The remainder of the body I would expect to show only the changes secondary to cardiac failure such as liver engorgement.

Pathologic Discussion

DR. PRICHARD: Dr. Gilmour has come as close to the diagnosis as I would think humanly possible. I say "has come close to the diagnosis" advisedly, since when I tell you that our principal diagnosis was idiopathic myocarditis I have not said a great deal. The immediate cause of death was embolism of the right middle cerebral artery, which had produced infarction of the right parietal and occipital lobes. The embolus had originated from a mural thrombus attached to the left ventricular wall. There were also infarcts in the kidneys and spleen. The heart was moderately enlarged (660 Gm.), markedly dilated, and without

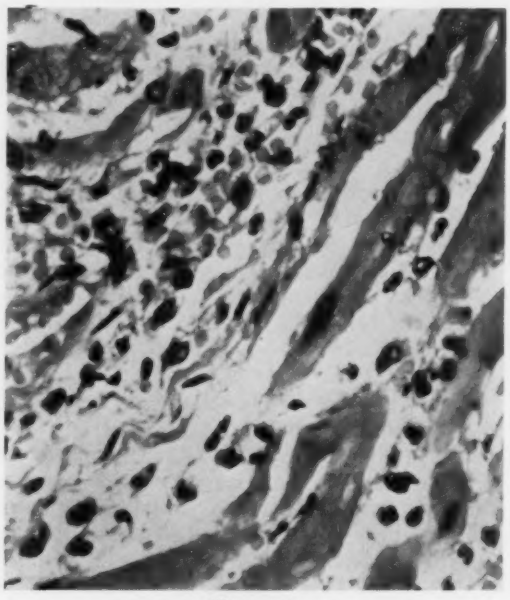


Figure 2

valvular lesions or significant coronary artery disease. The other autopsy findings were nonspecific and noncontributory to this presentation.

Microscopically there were poorly outlined, small foci of coagulation necrosis of myocardial fibers, with moderate numbers of neutrophilic granulocytes and cardiac histiocytes interspersed with erythrocytes and prominent fibrocytes. In some foci there was a moderate amount of collagen deposition, and only a few of the cells mentioned above. The inflammatory process also involved the epicardium and endocardium to a minor degree, and one might properly refer to the entire process as pancarditis.

The subject of myocarditis is not a very satisfactory one for discussion, since very little is known about cases of the present type; probably due, in part at least, to their rarity. It is sometimes difficult to realize that it was not so very long ago that myocarditis was diagnosed with considerable frequency, largely because postmortem examinations were inadequate. Most of the "myocarditis" of years past would be recognized as myocardial infarction today.

There is much confusion over classification and terms in myocarditis, and to delve into this problem would be beyond the scope of this discussion. The excellent review of Saphir, a dissertation of 100 pages, examines the general question in great detail. There are recognized entities which produce myocarditis, rheumatic fever being the most common in all probability, and diphtheria serving as an example of infectious disease producing important degenerative and inflammatory changes in the myocardium. There is presumptive evidence which connects various drugs to myocarditis, and sulfanomides have been rather extensively belabored from this standpoint; in each instance there is a strong element of *post hoc* reasoning. After all conceivable etiologic agents have been eliminated, there remains a group of myocardial inflammatory lesions which have very little distinctive about them. Some occur in infants, and some in older people, like the present patient. I see no point in appending "Fiedler's" myocarditis to the diagnosis of this patient, since it adds nothing to our understanding of the disease, even if it does have a familiar ring. The significance of the rather vague respiratory illness which was a feature during this man's clinical course is unknown to me. It does not seem to have been severe enough to have an important relationship to his myocarditis, and there is a great deal of subjectivity in any evaluation of such ailments.

1. Saphir, O: Myocarditis, Arch. Path. 32:1000-1051 (Dec.) 1941; 33:88-137 (Jan.) 1942.

Committees and Organizations

North Carolina Department of Public Health

The enlargement of programs to deal with chronic diseases tops the list of North Carolina's public health needs for 1960.

Compulsory immunization for poliomyelitis is viewed as the outstanding public health achievement of 1959.

During the first week of January Dr. J. W. R. Norton, State Health Director, took a look at problems and programs for the New Year as the staff of the State Board of Health reviewed achievements for the past twelve months.

The increasing industrialization of North Carolina has pointed up the presently inadequate facilities for occupational health services from the State Board of Health to the industries of North Carolina. The need for an enlargement of this service to the State is becoming increasingly recognized.

Passage by the 1959 General Assembly of compulsory immunization against poliomyelitis made North Carolina the first State in the Nation to enact this legislation, Dr. Norton stated.

Among other achievements of the past year were: the recognition by the General Assembly of the importance of the State Board's program of accident prevention; the extension of public health nursing services to the chronically ill in local health jurisdictions financially able to set up such a program; and the strengthening of the cooperation between the State Hospitals and the State Mental Health Authority.

Turning to newly emerging health problems and the longstanding needs in public health in North Carolina, Dr. Norton underlined the urgent need for the enlargement of the program of mental health services to families. Other newly emerging health problems in North Carolina which directly affect the citizens are noted as: staphylococcal infections occurring in nursing homes and hospitals, and the need for more adequate protection of private water supplies from chemical pollution. Migrant labor health problems and the extension of studies involving occupational hazards and involving alcoholism were also listed among the important emerging health problems. The study of atomic and nuclear programs as they affect

health administrative procedures will be important.

Longstanding public health problems challenging the State, as given by Dr. Norton included: expansion of chronic disease research work, health care of the aged, the great difficulty in recruitment and retention of qualified health personnel and the lack of adequate financial resources in all health areas at both state and local levels.

The increasing cost of medical care and hospitalization is seen as a problem both of longstanding and increasing importance. This increasing cost is resulting in inability of many families to obtain adequate health services.

North Carolina has created a demand for dental services which cannot be met promptly with present personnel and resources in either the field of private practice or public health, Dr. Norton stated.

Shortages in personnel exist in all areas of health care. The state is thirty-ninth in the ratio of physicians to population and forty-second with respect to dentists. The shortages are equally serious in public health personnel in all positions.

If adequate personnel and finances were available in North Carolina, the most important expansion in program, according to Dr. Norton, would be focused on protection and maintenance of adult health in an organized administered manner. This would form the basis of an added strengthening of the human and material resources and the total economy of the State, Dr. Norton stated.

"The State as a whole prospers, when, through good adult health, individuals and families and the communities prosper in ways that permit profitable and productive work," Dr. Norton concluded.

Classified Advertisements

WANTED: Male psychiatrist; Diplomate or with three years approved training; to join group practice 145-bed approved psychiatric hospital. Salary: $15,000-$18,000 first year; $20,000-$25,000 second with incentive factor. Write Box 790 care this Journal, Raleigh, N. C.

ONE UROLOGICAL TABLE with x-ray equipment for sale. Write Douglas Hamer, Jr., M.D., Box 658, Lenoir, N. C.

GENERAL PRACTITIONER for agricultural and industrial supported rural community of eight thousand in Eastern North Carolina. L. A. Gardner, Chrm. Medical Service Committee, Saratoga Lions Club, Saratoga, N. C.

DESIRABLE LOCATION for a physician. Contact Godley Realty Company, Mt. Holly Road, Charlotte, North Carolina.

BULLETIN BOARD

COMING MEETINGS

Medical Society of the State of North Carolina, One Hundred Sixth Annual Session — Raleigh, April 8-11.

Greensboro Academy of Medicine—Greensboro, March 24.

Ninth Annual Cancer Symposium, sponsored by the Forsyth County Medical Society in cooperation with the Forsyth Cancer Service—Winston-Salem, March 31.

Eighth Annual North Carolina Hospital Food Service Institute—North Carolina State College, Raleigh, April 6-8.

First Physicians' Institute on Alcoholism—University of North Carolina School of Medicine, Chapel Hill, April 6 (2:00-6:00 p.m., followed by dinner and reception).

New Hanover County Medical Symposium—Cape Fear Country Club, Wilmington, April 8.

American College of Chest Physicians, Thirteenth Annual Postgraduate Course in Diseases of the Chest—Sheraton Hotel, Philadelphia, March 14-18.

American Academy of General Practice, Twelfth Annual Scientific Assembly—Philadelphia, March 21-24.

Chicago Committee on Trauma of the American College of Surgeons, Fourth Postgraduate Course on Fractures and Other Trauma—Chicago, April 27-30.

NEW MEMBERS OF THE STATE SOCIETY

The following physicians joined the Medical Society of the State of North Carolina during the month of January.

Dr. John W. Barnard, Banner Elk; Dr. Robert Clement Smith, Banner Elk; Dr. Jack Bernard Perkins, P. O. Box 1027, Southport; Dr. Claude Benjamin Goswick, Jr., 726 5th Avenue, W., Hendersonville; Dr. Arthur Sherman Morris, Jr., P. O. Box 25, Hot Springs; Dr. John F. Ditunno, Jr., Hot Springs.

NEWS NOTES FROM THE DUKE UNIVERSITY MEDICAL CENTER

Establishment of a new training and research program at Duke University to provide for effective collaboration between the social sciences and health fields has been announced by Dr. Paul M. Gross, vice-president in the Division of Education.

The program is headed jointly by Dr. John C. McKinney, chairman of the Department of Sociology, who has received the additional title of professor of medical sociology; and Dr. Ewald W. Busse, chairman of the Duke Medical Center's Psychiatry Department.

The appointment of Charles C. Boone as one of two assistant superintendents of Duke Hospital has been announced by hospital superintendent Charles H. Frenzel.

Succeeding the late Dewitt Wright, who died on August 10, 1959, Boone assumed his new position on January 26. He was formerly administrator of Barnwell County Hospital, South Carolina.

* * *

H. D. Maynard Jr. has been named assistant business manager of the surgical division of Duke Hospital's Private Diagnostic Clinic.

He will assume a position left vacant by Lewis W. Sykes, who has resigned effective December 31 to become business manager of the Miller Orthopedic Clinic in Charlotte.

* * *

A new clinic for children and young people afflicted with cystic fibrosis has been organized at the Duke University Medical Center.

Cystic fibrosis, a relatively common hereditary disease which affects the lungs and pancreas, has been recognized only within the past 20 years. Before the introduction of "miracle" antibiotics, few persons with the disease lived beyond 14 years of age.

The new Duke clinic is headed by Dr. Susan C. Dees, professor of pediatrics, and Dr. A. Douglas Rice, instructor in pediatrics. Working with them are other Duke pediatricians and members of the Medical Center's dietetics and physical therapy staffs.

News Notes from the University of North Carolina School of Medicine

Dr. Kenneth M. Brinkhous, professor and head of the Department of Pathology, is the editor of a new book concerning an international medical meeting held in Rome in September.

The book, entitled "Hemophilia and other Hemorrhagic States," has just been released by the University of North Carolina Press.

The U.N.C. School of Medicine has long been known as one of the world's leading centers for the study of hemophilia and other bleeding diseases. The world's only colony of dogs that have hemophilia is located at the School of Medicine.

* * *

A capacity enrollment of 50 Tar Heel physicians attended a three-day course in pediatric cardiology at the University of North Carolina School of Medicine January 13-15.

Instructors for the course, in addition to a number of the faculty members of the U.N.C. School of Medicine, were Dr. Edward C. Lambert of the University of Buffalo School of Medicine and Dr. Robert F. Castle of the Duke University School of medicine.

Two leaves of absence and one appointment in the University of North Carolina School of Medicine have been announced by Chancellor William B. Aycock.

Dr. Charles H. Burnett, professor and head of the Department of Medicine, has been granted a one-year leave of absence beginning July 1. Dr. Burnett will be engaged in research in London at the University of London and the Galton Laboratory for Human Eugenics.

Dr. Carl W. Gottschalk will receive a year's leave at the same time. He will be engaged in research at the Biochemical Institute of the University of Copenhagen, Denmark.

Dr. A. J. Bambara has been appointed a U. S. Public Health Service practitioner trainee in the Department of Psychiatry.

* * *

A research grant in the amount of $79,953 (for a three-year period) has been awarded by the National Institute of Mental Heath to Dr. Hans H. Strupp, associate professor of psychology and director of psychological services in the Department of Psychiatry. This research will concern the role and function of the psychotherapist's personality and attitudes in the psychotherapeutic process. The work has been in progress since 1955, and is carried out in collaboration with Joan V. Williams, Ph. D., and Martin S. Wallach, Ph. D.

* * *

The appointment of Rachel L. Nunley to the State Examining Committee of Physical Therapists was announced recently by Governor Hodges.

Miss Nunley, an instructor in physical therapy at the University of North Carolina School of Medicine, will serve a three-year term, succeeding Margaret Moore, chief physical therapist of the North Carolina Memorial Hospital.

* * *

North Carolina Memorial Hospital has been awarded a grant of $114,494 by the General Medical Services Division of the National Institute of Health of the United States Public Health Service. The grant will finance a four-year research project entitled "Improving Hospital Physician Relations Through Education." Dr. Robert R. Cadmus, director of the Hospital and professor of hospital administration of the School of Medicine, will serve as principal investigator.

The purpose of this study is to develop with the existing medical curriculum an effective program of instruction which will provide to the maturing medical student a better understanding of the administrative implications of the practice of medicine, particularly in the hospital setting. It is hoped that with increased knowledge and with the development of sound and mutually acceptable concepts, these relationships can be strengthened on a national level.

Four women technicians in x-ray technology received certificates recently to mark the completion of a 15-month course in radiology sponsored by North Carolina Memorial Hospital.

The four are Nancy Lanier Green, Durham; Violet Sue Stancil, Kenly; Joyce Gayle Strickland, Wilmington; and Alice Louise Teague, Liberty.

* * *

University of North Carolina President William C. Friday was announced recently as a member of a special board to choose Markle Scholars—outstanding young doctors in medical schools in the United States and Canada.

The Markle Foundation of New York, which makes 25 awards a year of $30,000 each to young physicians and surgeons, stated that President Friday will serve on the Markle Selections Committee for seven western states.

News Notes from the Bowman Gray School of Medicine of Wake Forest College

A Department of Neurology has been established at Bowman Gray. Heretofore neurology has functioned as a section of the Department of Psychiatry. The Board of Trustees has approved Dr. Martin G. Netsky, who has been in charge of the Neurology Section for the past four years, as chairman of the new department.

In establishing this new department, the Board of Trustees took note of the broad scientific and educational contributions and the growing importance of neurology in this institution. The staff of the Department of Neurology has participated in educational programs of undergraduate medical students in all four years, has developed strong programs at the graduate level in neurology and pediatric-neurology, and is now engaged in extensive and varied research activities.

* * *

Dr. Harold D. Green, professor of physiology and pharmacology, has been appointed to the editorial board of **Circulation Research.** This appointment is for a period of five years.

* * *

Dr. Samuel H. Love, instructor in microbiology and immunology, has returned after a year's leave of absence. During that time he was associated with the Department of Biochemistry at the University of Pennsylvania School of Medicine, where he was engaged in study of growth and cell differentiation from the biochemical viewpoint, utilizing tissue culture techniques.

* * *

The North Carolina Heart Association awarded Grants-in-Aid totaling $9,132.00 to the following faculty members of the Bowman Gray School of Medicine: Drs. John LeMay, J. Maxwell Little, Jesse Meredith, Henry Miller, Joseph Whitley, and Nancy O'Neil Whitley.

Forsyth County Cancer Symposium

The ninth annual cancer symposium sponsored by the Forsyth County Medical Society and the Forsyth Cancer Service will be presented at the Hotel Robert E. Lee in Winston-Salem on March 31.

The following tentative program, entitled "Cancer in Childhood," has been arranged.

1:00 p.m.—Registration

1:15 p.m.—Symposium called to order
Invocation—Dr. Mark Depp, Centenary Methodist Church
Welcome—**Dr. Charles R. Welfare,** President Forsyth County Medical Society
Mrs. Fred P. Crouch, President Board of Directors Forsyth Cancer Service

1:30 p.m.—Basic biological features in childhood cancer
Dr. James B. Arey, Associate Professor of Pathology, Temple University, Pa.

2:00 p.m.—Childhood leukemia and related diseases
Dr. Nathan J. Smith, Professor of Pediatrics, University of Wisconsin, Madison, Wisconsin

2:30 p.m.—Cancer of the genito-urinary tract in childhood
Dr. Albert J. Paquin, Professor of Urology, University of Virginia, Charlottesville, Va.

3:15 p.m.—Panel Discussion
Dr. Eben Alexander, Jr., professor of neurology, Bowman Gray School of Medicine, will join the other speakers for this panel.

7:00 p.m. Dinner—Ballroom
Speaker: Dr. W. C. Davison
Presiding—Dr. Charles R. Welfare

Greensboro Academy of Medicine

The following program has been arranged for the Greensboro Academy of Medicine to be held on Thursday, March 24.

"The Therapeutic Use of Radio Isotopes"—Manuel M. Garcia, M.D., Professor of Radiology, Tulane University School of Medicine, New Orleans

"Massive Hemorrhage From The Lower Gastrointestinal Tract: Diagnosis & Treatment"—Rudolf Noer, M.D., Professor of Surgery, University of Louisville, Louisville

"Perinatal Mortality"—D. Frank Kaltreider, M.D., Professor of Obstetrics, University of Maryland, Baltimore

"Congenital Heart Disease"—Allen Friedlich, M.D., Associate Professor of Medicine, Harvard Medical School, Boston

"Extent of Cancer Illness in the United States"

—Michael Shimkin, M.D., National Institute of Cancer, Bethesda, Maryland

"The Tired Mother Syndrome"—Leonard Lovshin, M.D. (after dinner), Cleveland Clinic, Cleveland, Ohio

New Hanover Medical Society

The New Hanover County Medical Symposium, held previously at Wrightsville Beach in July, will be presented this year on April 8 at the Cape Fear Country Club. The following program has been announced.

I—Panel Discussion on Tobacco and Cancer
- 1—Dr. Alton Ochsner—Surgeon in chief—Ochsner Clinic
- 2—Dr. Douglas Sprunt—Professor of Pathology—University of Tennessee
- 3—Representative from the Tobacco Industry —Moderator Dr. George Lumb

II—Panel Discussion on Death and Its Legal Consequences.
- 1—Dr. Milton Helpern—Chief Medical Examiner—New York City
- 2—Mr. Malcolm Seawell, Attorney General—State of North Carolina
- 3—Dr. Douglas Sprunt—Professor of Pathology—University of Tennessee

Moderator, Mr. Aaron Goldberg

III—Panel Discussion on the Thyroid Gland
- 1—Dr. Milton Hamolsky, Assistant Professor of Medicine Harvard Medical School
- 2—Dr. R. M. Hill, Assistant Professor of Medicine, University of Alabama
- 3—Surgeon to be announced

Moderator—Dr. Samuel Warshauer

Robeson County Medical Society

The Robeson County Medical Society held its monthly meeting on February 1 at Johnson's Restaurant in Lumberton. The program was sponsored by the Robeson County Unit of the American Cancer Society. Dr. Damon Blake, director of radiotherapy, Bowman Gray School of Medicine spoke on the use of cobalt therapy in the treatment of cancer.

The executive committee of the county unit of the American Cancer Society were guests of the society at the meeting.

Forsyth County Medical Society

The regular dinner meeting of the Forsyth County Medical Society was held on February 9 at the Hotel Robert E. Lee. Mr. C. W. Johnson, chief federal agent of the Narcotic Division, Greensboro, discussed the problem of narcotic addiction. A sound film was shown in connection with the discussion.

Edgecombe-Nash Medical Society

The Edgecombe-Nash Medical Society met on January 13 at the Rio Restaurant in Rocky Mount. Dr. C. T. Smith was in charge of the program and introduced as speaker Dr. George Andrews of the Dorothea Dix Hospital, whose subject was preventive psychiatry.

Officers of the society for 1960 are as follows: Dr. J. G. Chamblee, president; Dr. O. E. Bell, president-elect; Dr. J. C. Brantley, Jr., first vice president; Dr. L. W. Robertson, second vice president; Dr. J. M. Warren, secretary and treasurer; Dr. N. B. Carter, editor of the Bulletin.

News Notes

Dr. Donald B. Koonce and Dr. John B. Codington of Wilmington have announced their association in the practice of general surgery, with offices at 408 Eleventh Street.

Tri-State Medical Association

Annual Meeting, March 21 and 22, 1960, Columbia Hotel, Columbia, South Carolina.

Program

Monday, March 21

9:30 a.m.—"Current Medical Treatment of Hyper-Cholesterolemia and Hyperlipemia and Atherosclerosis"—Dr. Edwin Boyle, Jr., Charleston, S. C.

10:00 a.m.—Paper—"Recent Surgical Developments in Hypertension and Peptic Ulcer,"—Dr. Keith S. Grimson, Durham, N. C.

11:00 a.m.—Paper—"What Do Simple Kidney Function Tests Mean?"—Dr. Cheves McC. Smythe, Charleston, S. C.

11:30 a.m.—Paper—"Neurological Complications of Disease of the Cervical Spine,"—Dr. Rhett Talbert, Charleston, S. C.

12:00 Noon—Paper—"Diagnosis and Medical Management of Bleeding Esophageal Varices"—Dr. Malcolm P. Tyor, Durham, N. C.

12:30 to 2:00 p.m.—Luncheon Panel
Dr. Keith Grimson, Moderator, Dr. Edwin Boyle, Jr., Dr. Cheves McC. Smythe, Dr. Rhett Talbert, and Dr. Malcolm P. Tyor

2:00 p.m.—Paper—"Pulmonary Alveolar Proteinosis"—Dr. William Schulze, Greenville, S. C.

2:30 p.m.—Paper—"The Role of Ascorbic Acid in Human Pathology"—Dr. Fred R. Klenner, Reidsville, N. C.

3:30 p.m.—Panel on Psychosomatic Medicine
(a) Dr. Charles Fulghum, Department of Psychiatry and Neurology, Emory University Medical College, Atlanta, Georgia

(b) "How the Treatment of Some of Aged Psychotics Can be Effective"—Dr. James Asa Shield, Chief of Department of Psychiatry and Neurology, Medical College of Virginia, Richmond, Va.
(c) "Somatophysic Manifestations of Disease"—Dr. Vince Moseley, Chief of Department of Medicine, Medical College of South Carolina, Charleston, S. C.
(d) "Psychosomatic Problems in General Practice"—Dr. William Hendrix, President of S. C. Chapter of the American Academy of General Practice, Spartanburg, S. C.
(e) General discussion by Drs. Fulghum, Shield, Moseley and Hendrix with questions from the floor.

Tuesday, March 22

8:30 a.m.—Paper—"Blood Sugar and Urine Sugar Determinations in the Diagnosis and Management of Diabetes"—Dr. William R. Jordan, Richmond, Va.

9:00 a.m.—Paper—"Office Urology"—Dr. Kenneth M. Lynch, Jr., Charleston, S. C.

9:30 a.m.—Paper—"Surgical Treatment of Facial Injuries"—Dr. C. C. Coleman, Jr., Charlottesville, Va.

10:00 a.m.—Paper—"Endocrine Therapy In General Practice"—Dr. J. Richard Sosnowski, Charleston, S. C.

11:00 a.m.—Paper—"The Treatment of Congestive Heart Failure"—Dr. Paul D. Camp, Richmond, Va.

11:30 a.m.—Paper—"The Treatment of Electrolyte Emergencies"—Dr. Dana C. Mitchell, Jr., Columbia, S. C.

12:00 Noon—Paper—"Diagnostic and Treatment of Respiratory Infections in Children"—Dr. George Dean Johnson, Spartanburg, S. C.

12:30 to 2:00 p.m.—Luncheon—Panel
Dr. C. C. Coleman, Jr., Moderator, Dr. Paul D. Camp, Dr. Kenneth M. Lynch, Jr., Dr. Dana C. Mitchell, Jr., Dr. George D. Johnson, Dr. J. Richard Sosnowski and Dr. William R. Jordan.

2:00 p.m.—Paper—"Problems in Immunization Against Infectious Diseases"—Dr. Samuel F. Ravenel, Greensboro, N. C.

3:00 to 4:30 p.m.—Panel on Thyroid Disease
(a) "Problems in Diagnosis and Treatment of Thyroid Disease"—Dr. William H. Prioleau, Moderator, Clinical Professor of Surgery, Medical College of S. C., Charleston, S. C.
(b) "Medical Evaluation in Thyroid Disease"—Dr. Ben N. Miller, Senior Visiting Staff, Internal Medicine, Columbia Hospital, Columbia, S. C.
(c) "Pathological Pitfalls in the Diagnosis of Thyroid Lesions"—Dr. Rawling Pratt-Thomas, Professor of Pathology, Medical College of South Carolina, Charleston, S. C.
(d) "Behavior of the Thyroid During Pregnancy"—Dr. Luther Talbert, Department of Obstetrics and Gynecology, University of North Carolina, Chapel Hill, N. C.
(e) General Discussion by Drs. Priolear, Miller, Pratt-Thomas and Talbert with questions from the floor.

SOUTHERN MEDICAL ASSOCIATION

Robert F. Butts, Birmingham, business manager of Southern Medical Association, has been named executive secretary-treasurer of the 14,000-member association. He also retains his duties as business manager.

The announcement was made by Dr. Edwin Hugh Lawson, New Orleans, president of the S.M.A. following a meeting of the association's executive committee.

Dr. Lawson also announced the appointment of V. O. Foster, Birmingham, as professional relations counselor. C. P. Loranz, Birmingham, remains as adviser and special consultant, Dr. Lawson said.

Southern Medical maintains home office-headquarters at 2601 Highland Avenue, Birmingham. Its fifty-fourth annual meeting will be held in St. Louis, Missouri, October 31-November 3 of this year.

SOUTHERN MEDICAL ASSOCIATION

Section on Ophthalmology and Otolaryngology

At the meeting of the Southern Medical Association held in Atlanta on November 15-19, 1959, the following officers were elected for the Section on Ophthalmology and Otolaryngology for the coming year:

Chairman, Dr. George M. Haik, Professor and Head of the Department of Ophthalmology at Louisiana State University School of Medicine, 812 Maison Blanche Building, New Orleans 16, Louisiana.

Chairman-elect, Dr. Mercer G. Lynch, Assistant Professor of Otolaryngology, Tulane University School of Medicine, 3503 Prytania Street, New Orleans 15, Louisiana.

Vice-Chairman, Dr. Bernard J. McMahon, Director of the Department and Clinical Professor of Otolaryngology, St. Louis University School of Medicine, 8230 Forsythe Blvd., Clayton 24, Missouri.

Secretary, Dr. Albert C. Esposito, First Huntington National Bank Building, Huntington, West Virginia, formerly instructor of ophthalmology,

Ohio State Universiy College of Medicine, Columbus, Ohio.

The next meeting of the Section will be held in St. Louis, Missouri, from October 31 to November 3, 1960. Those interested in participating should write to the Secretary of the Section, Dr. Albert C. Esposito.

American College of Chest Physicians (Southern Chapter)

At the annual meeting of the Southern Chapter of the American College of Chest Physicians, held in Atlanta, Georgia, November 15-16, 1959, the following officers were elected: president—John H. Seabury, M.D., New Orleans, Louisiana; first vice-president—DeWitt C. Daughtry, M.D., Miami, Florida; second vice president—Henry R. Hoskins, D., San Antonio, Texas; secretary-treasurer—Joseph W. Peabody, Jr., M.D., Washington, D.C.

American College of Surgeons

A grant of $146,275 by The John A. Hartford Foundation, Inc., of New York, to the American College of Surgeons to inaugurate a program for improving the medical management of the surgical and injured patient was announced recently Mr. Ralph W. Burger, president of the Foundation and Dr. I. S. Ravdin, chairman of the Board of Regents of the College.

American Board of Obstetrics and Gynecology

Then next scheduled examinations (Part II), oral and clinical, for all candidates will be conducted at the Edgewater Beach Hotel, Chicago, Illinois, by the entire Board from April 11 through 16. Formal notice of the exact time of each candidate's examination will be sent him in advance.

Candidates who participated in the Part I Examinations will be notified of their eligibility for the Part II Examinations as soon as possible.

The deadline date for the receipt of New and Reopened Applications for the 1961 examinations is August the first 1960. Candidates are urged to submit their applications as soon as possible before that time.

The World Medical Association

The German Medical Association, host of the fourteenth General Assembly of the World Medical Association, scheduled to convene in West Berlin, September 15-22, 1960, has extended a cordial invitation to all the doctors of the world to attend this outstanding meeting.

Additional information including programs and schedules will be available on or about March 1 at the W.M.A. Headquarters Secretariat. Request should be addressed to: The World Medical Association, 10 Columbus Circle, New York 19, New York.

The National Association of Blue Shield Plans

More than 1,600,000 persons enrolled in the 73 Blue Shield Plans located in North America during the first nine months of 1959, and during the same period Blue Shield paid out over $487,500,000 for medical-surgical care rendered to members, the National Association of Blue Shield Plans reported today.

The nationwide Blue Shield Plans and their sponsoring medical societies have registered outstanding progress in implementing the American Medical Association resolution—passed December 4, 1958—calling for the development of medical care coverage for the aged by voluntary means, John W. Castellucci, executive vice president of the National Association of Blue Shield Plans said recently in Chicago.

"We have just completed a special survey in order to determine the progress made by Blue Shield Plans since the passage of the AMA resolution last December 4 and the results are most encouraging," Castellucci reported.

"Only eight of the 67 Blue Shield Plans located in the United States, with only two per cent of total Blue Shield membership, have no programs for senior citizens in the works at the present time," he noted.

The Month in Washington

Overshadowing all other developments from the standpoint of the medical profession was the flat prediction from a high Administration official and key lawmakers that Congress this year would vote some sort of liberalization of the Social Security program.

There was general agreement that Congress would broaden the Social Security plan for permanently and totally disabled persons by removing the requirement that a person has to be at least 50 years of age before receiving such benefits.

However, there were forecasts of even further liberalization. House Speaker Sam Rayburn (D., Texas.) said monthly cash benefits also may be boosted. On the other hand, the House leader said he believed a majority of the House Ways and Means Committee were opposed to the disputed Forand bill that would finance partial health care for the elderly through higher Social Security taxes at an estimated extra cost of $2 billion annually. As a result, he said, he did not think "there was a great deal of chance for it." But the AFL-CIO

From the Washington Office of the American Medical Association, 1523 L Street, N. W.

and some Congressional backers of the highly controversial bill were urging Congress to approve it this year.

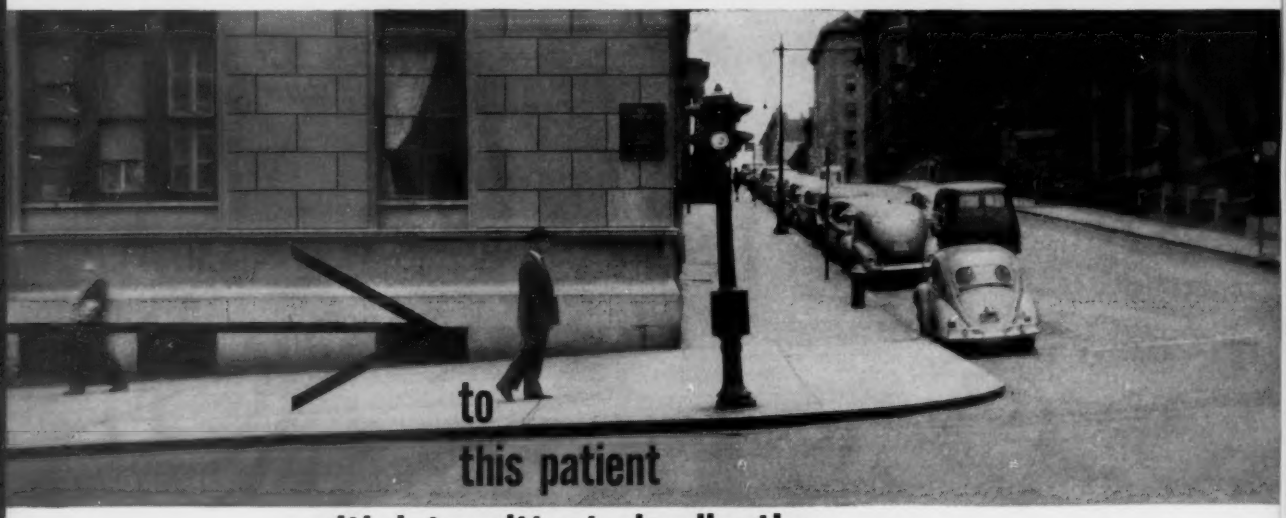
Arthur S. Flemming, Secretary of Health, Education and Welfare, asserted that the Administration is planning to offer a program aimed at assisting needy aged to meet health bills, but gave no details. The official noted that the Administration has firmly opposed the Forand-type approach on grounds it would destroy the rapid progress in meeting the problem through private means. But Flemming, in a speech before the American Association of University Teachers of Insurance, said the Administration has an obligation "to stay with it" until it arrives at a plan.

Congress has extended the Social Security program every presidential election year since 1948, and 1960 appeared to be no exception. Whether or not the issue of medical care for the aged will be included was one of the big question marks early in the session.

Shortly before Congress convened, the Boards of Trustees of the A.M.A. and the American Hospital Association, in a joint resolution, pledged to "mobilize their full resources to accelerate the development of adequately financed health care programs for needy persons — especially the aged needy—" at state and local levels

The Boards said Forand-type legislation is "not designed to assist to the needy, since they apply to all Social Security beneficiaries and exclude the majority of needy persons, who are not eligible for Social Security benefits."

Following the action, Dr. Louis M. Orr, A.M.A. President, and three other A.M.A. officials—Dr. E. Vincent Askey, President-Elect, Dr. F. J. L. Blasingame, Executive



with intermittent claudication
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makes the blocks so much shorter...
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Vice President, and Dr. Ernest B. Howard, Assistant Executive Vice President—visited Vice President Richard M. Nixon at his Washington Office. They told the Vice President that by the end of this year an estimated 60 per cent of the nation's aged persons who want and need voluntary health insurance will have it.

Mr. Nixon, according to the officials, was delighted to receive the information and "very much interested" in the program of voluntary health insurance for the aged.

In Memoriam

Oscar Julian Houser, M.D.

WHEREAS, Dr. Oscar Julian Houser was born December 27, 1885, and died July 21, 1959.

He was educated in the schools of Gaston County and the North Carolina Medical College from which he graduated in 1914. He engaged in the general practice of medicine until 1921. He then took a graduate course in eye, ear, nose and throat at the Manhattan Hospital and the New York Postgraduate Clinic. He returned to Charlotte and followed this specialty until his death. During his span of life he gave wholeheartedly to his profession and to his church, and therefrom gained many firm and lasting friendships.

Therefore, be it Resolved, That the Mecklenburg County Medical Society has lost a valuable member and that he will be greatly missed by his colleagues; and that we, the members of the Mecklenburg County Medical Society express our deep sorrow and extend our sympathy to his bereaved family; and that a copy of these RESOLUTIONS be placed in the permanent files of this Society; and that a copy be sent to his family.

C. L. Nance, M.D., Chairman
H. L. Newton, M.D.
R. B. McKnight, M.D.

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Arlidin is available in 6 mg. scored tablets, and 5 mg. per cc. parenteral solution. See PDR for dosage and packaging.

Protected by U. S. Patent Numbers: 2,661,372 and 2,661,373

Henry Lee Sloan
1886-1959

Henry Sloan was born in Ingold, North Carolina, August 6, 1886, the son of Dr. Henry and Catherine (Boykin) Sloan.

He attended the University of North Carolina, graduating with the degree of Bachelor of Arts in 1907, and received the degree of Doctor of Medicine from the University of Pennsylvania in 1911.

Postgraduate training was obtained at the Presbyterian Hospital in Philadelphia, Pennsylvania and at the New York Eye and Ear Infirmary.

He located in Lincolnton, North Carolina, where he practiced general medicine for one year and then became associated with the late Dr. J. P. Matheson and the late Dr. C. N. Peeler in the founding of the Charlotte Eye, Ear and Throat Hospital in 1923.

Dr. Sloan was a pioneer in ophthalmology in this area; and his interest, his enthusiasm, and his scientific achievement was widely acclaimed.

He maintained a keen interest in medical affairs, served as President of the Mecklenburg County Medical Society, was active in the affairs of the North Carolina State Medical Society, and received its Moore County Medal Award in 1926. He maintained an active interest in the American Academy of Ophthalmology and Otolaryngology and served on its regional committee for selection of candidates to the Society.

Dr. Sloan was married to Emily Patterson Elliott in 1919. Born to them were a daughter, Jane Elliott, now residing in Pittsburgh, Pennsylvania, and a son, Henry Lee Sloan Jr., an ophthalmologist associated with the Charlotte Eye, Ear and Throat Hospital. Emily died in 1947.

In 1951 he married Eleanor Clarke Bullard who survives him.

Henry Sloan was greatly endowed with charm and grace of manner which endeared him to a large circle of friends and confreres who were deeply sorrowed by his death November 5, 1959.

J. S. Gaul
Joseph A. Elliott
V. K. Hart

Dave Hebrank Smeltzer
November 7, 1921—July 22, 1959

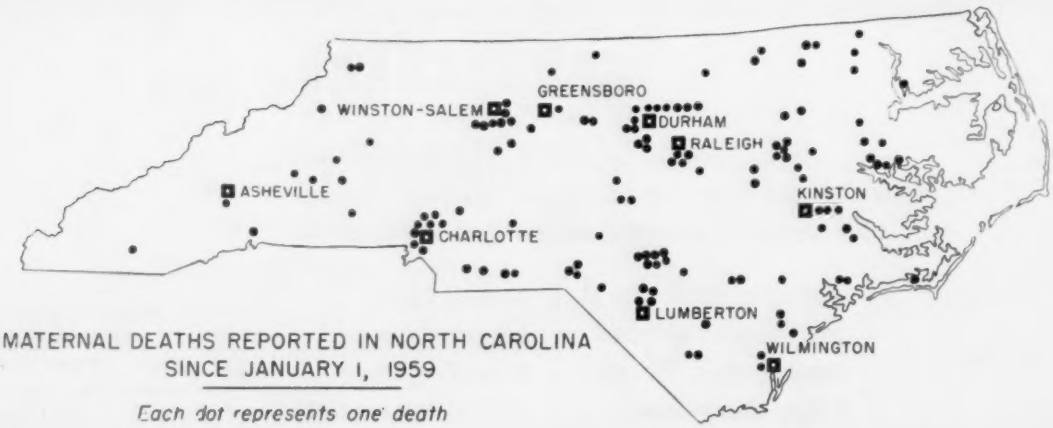
In the death of Dave H. Smeltzer on July 22, 1959, the Mecklenburg County Medical Society and citizens of our community lost a good friend, physician and loyal public servant.

Dr. Smeltzer was born November 7, 1921 in Youngstown, Ohio. He graduated from Rayen High School there in 1939, and received his A. B. degree from Duke University in 1943. His medical education was interrupted by four years of active duty with the United States Navy, following which he returned to Duke University and received his M.D. degree in 1950. From July, 1950-52 he served a rotating internship and rotating residency at Charlotte Memorial Hospital. Dr. Smeltzer entered general practice in August, 1952, with his office located at 3312 Tuckaseege Road. He had been in practice seven years at the time of his death. It is with regret that we mark the passing of this young physician and friend.

Dave is survived by one brother, his wife, the former Mildred James, and three children.

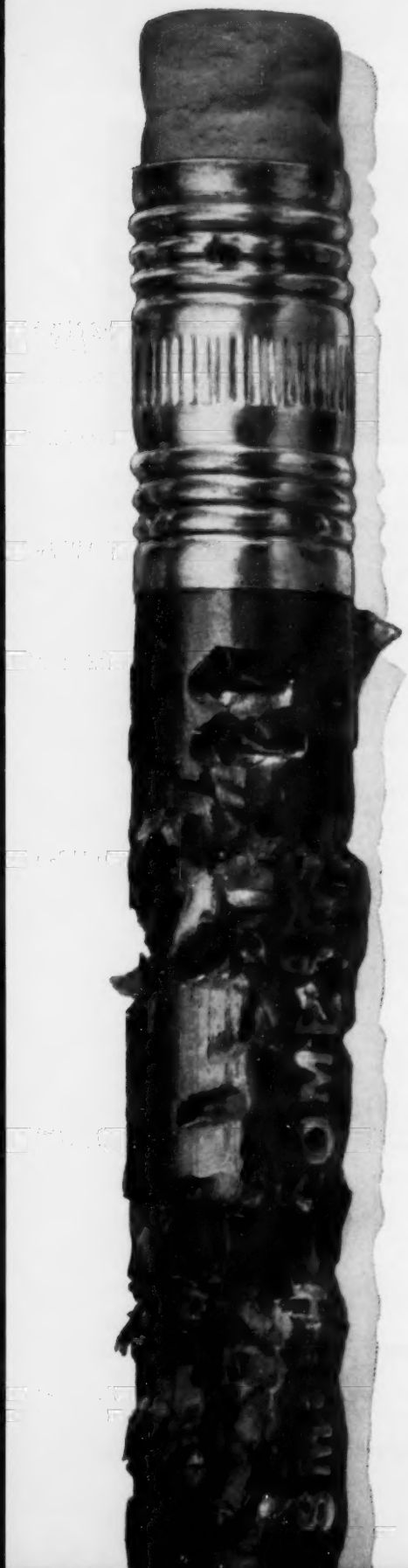
Be it therefore **Resolved** that a copy of this memorial be entered in the Minutes of the Mecklenburg County Medical Society, and copies be provided for his wife and his brother, Dr. James L. Smeltzer of Youngstown, Ohio, and the Medical Society of the State of North Carolina.

John M. Kester, M.D.



MATERNAL DEATHS REPORTED IN NORTH CAROLINA
SINCE JANUARY 1, 1959

Each dot represents one death



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properties

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broad-spectrum control in depth. Higher activity level enhances range of previous antibiotics. Some problem pathogens have been found more responsive. Strains of Pseudomonas, Proteus and *A. aerogenes* have proved sensitive to DECLOMYCIN.

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24-48 hours extra activity...protection against relapse. Antimicrobial control is maintained after stopping dosage. Most other antibiotics dissipate rapidly on withdrawal.

REFERENCES:

1-11. Papers read at Seventh Symposium on Antibiotics, Washington, D. C., November 4-6, 1959.

12. Phillips, F. M.: DECLOMYCIN—Seventh Interim Report. Department of Clinical Investigation, Lederle Laboratories, Pearl River, N. Y., December 4, 1959.

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Dosage: average adult, 1 capsule four times daily.

PEDIATRIC DROPS, 60 mg./cc. in bottle of 10 cc. with calibrated dropper.

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performance

genitourinary infection. Roberts, M. S.; Seneca, H., and Lattimer, J. K.,[1] New York, N. Y.—Ninety-one per cent of the Gram-positive and 27 per cent of the Gram-negative, among 66 organisms cultured from genitourinary infection, responded to DECLOMYCIN. Serum antibiotic activity was found three times greater than with tetracycline.

toleration. Boger, W. P., and Gavin, J. J.,[2] Norristown, Pennsylvania—Side effects with DECLOMYCIN were minimal. When dosage was 0.5 to 1 Gm. daily in divided doses, only two of 82 patients exhibited nausea.

activity level sustentation. Kunin, C. M.; Dornbush, A. C., and Finland, M.,[3] Boston, Massachusetts—Of the four tetracycline analogues, DECLOMYCIN Demethylchlortetracycline showed the longest sustained activity levels in the blood.

gonococcal infection. Marmell, M., and Prigot, A.,[4] New York, N. Y.—Of 63 cases of gonorrhea, 61 promptly responded after short courses of DECLOMYCIN. Therapeutic effect was found equal to that of intramuscular penicillin.

bronchopulmonary infection. Perry, D. M.; Hall, G. A., and Kirby, W. M. M.,[5] Seattle, Washington—Of 30 cases of acute bacterial pneumonia, all were afebrile following two to 10 days of treatment with DECLOMYCIN. Results were good in 21.... All of six patients with acute bronchitis responded promptly.

pediatric infection. Fujii, R.; Ichihashi, H.; Minamitani, M.; Konno, M., and Ishibashi, T.,[6] Tokyo, Japan—In 309 pediatric patients with various infections, DECLOMYCIN was effective in 75 per cent.

urogenital infection. Vineyard, J. P.; Hogan, J., and Sanford, J. P.,[7] Dallas, Texas—Clinical response in pyelonephritis correlated well with results of *in vitro* sensitivity tests, which showed some strains of *A. aerogenes*, Proteus and Pseudomonas more susceptible to DECLOMYCIN Demethylchlortetracycline than to its analogues.

pneumonia. Duke, C. J.; Katz, S., and Donohoe, R. F.,[8] Washington, D. C.—Results were satisfactory in all but two of 32 cases of acute bacterial pneumonia, of which only 11 were uncomplicated. No side effects were observed.

brucellosis. Chávez Max G.,[9] Mexico, D. F., Mexico—All of nine patients with *Br. melitensis* infection were afebrile after five days on DECLOMYCIN. Blood cultures were negative in all cases on the 20th day. Side effects were limited to slight temperature increases which abated in four days.

pustular dermatosis. Blau, S., and Kanof, N. B.,[10] New York, N. Y.—Results with DECLOMYCIN were excellent in both of two cases of impetigo, one of two cases of folliculitis, six of nine cases of furunculosis, all of three cases of acne rosacea and 26 of 45 cases of acne vulgaris. Overall, results were excellent or good in 85 per cent.

antibacterial spectrum. Finland, M.; Hirsch, H. A., and Kunin, C. M.,[11] Boston, Massachusetts—DECLOMYCIN Demethylchlortetracycline was found the most effective of the tetracycline analogues against two-thirds of 680 normally sensitive strains of 15 separate species.

the over-all picture. Combined results reported by 210 clinical investigators[12]—DECLOMYCIN produced a favorable response (cured or improved) in 87 per cent of 1,904 patients. Two-thirds of the patients received one capsule every six hours. Treatment was continued for as long as 180 days, but was between three and eight days in most. Side effects were seen in 9.9 per cent, but necessitated discontinuance of treatment in only 1.8 per cent.

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Diagnostic Quandaries

Colitis? Gall Bladder Disease?
Chronic Appendicitis?
Rheumatoid Arthritis? Regional Enteritis?

A DISEASE that is frequently overlooked in solving diagnostic quandaries is amebiasis. Its symptoms are varied and contradictory, and diagnosis is extremely difficult. In one study, 56% of the cases would have been overlooked if the routine three stool specimens had been relied on.[1]

Another study found 96% of a group of 150 patients with rheumatoid arthritis were infected by *E. histolytica*. In 15 of these subjects, nine stool specimens were required to establish the diagnosis.[2]

Webster discovered amebic infection in 147 cases with prior diagnoses of spastic colon, psychoneurosis, gall bladder disease, nervous indigestion, chronic appendicitis, and other diseases. Duration of symptoms varied from one week to over 30 years. In some cases, it took as many as six stool specimens to establish the diagnosis of amebiasis.[3]

Now treatment with Glarubin provides a means of differential diagnosis in suspected cases of amebiasis. Glarubin, a crystalline glycoside obtained from the fruit of *Simarouba glauca*, is a safe, effective amebicide. It contains no arsenic, bismuth, or iodine. Its virtual freedom from toxicity makes it practical to treat suspected cases without undertaking difficult, and frequently undependable, stool analyses. Marked improvement following administration of Glarubin indicates pathologically significant amebic infection.

Glarubin is administered orally in tablet form and does not require strict medical supervision or hospitalization. Extensive clinical trials prove it highly effective in intestinal amebiasis.

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TABLETS

specific for intestinal amebiasis

Supplied in bottles of 40 tablets, each tablet containing 50 mg. of glaucarubin.

Write for descriptive literature, bibliography, and dosage schedules.

1. Cook, J.E., Briggs, G.W., and Hindley, F.W.: Chronic Amebiasis and the Need for a Diagnostic Profile, Am. Pract. and Dig. of Treat. *6*:1821 (Dec., 1955).

2. Rinehart, R.E., and Marcus, H.: Incidence of Amebiasis in Healthy Individuals, Clinic Patients and Those with Rheumatoid Arthritis, Northwest Med., *54*:708 (July, 1955).

3. Webster, B.H.: Amebiasis, a Disease of Multiple Manifestations, Am. Pract. and Dig. of Treat. *9*:897 (June, 1958).

*U.S. Pat. No. 2,864,745

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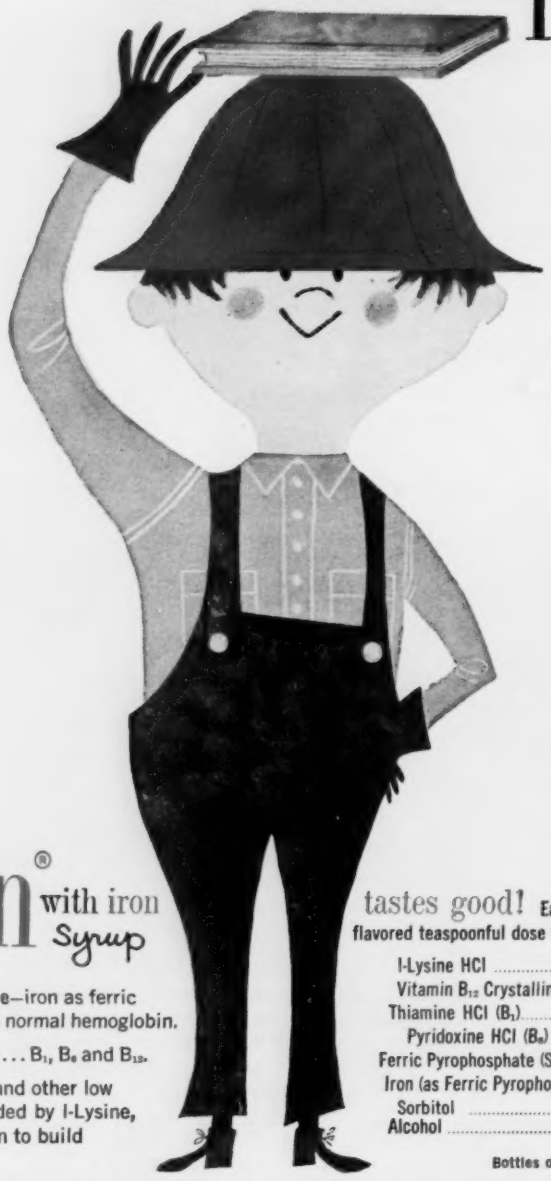

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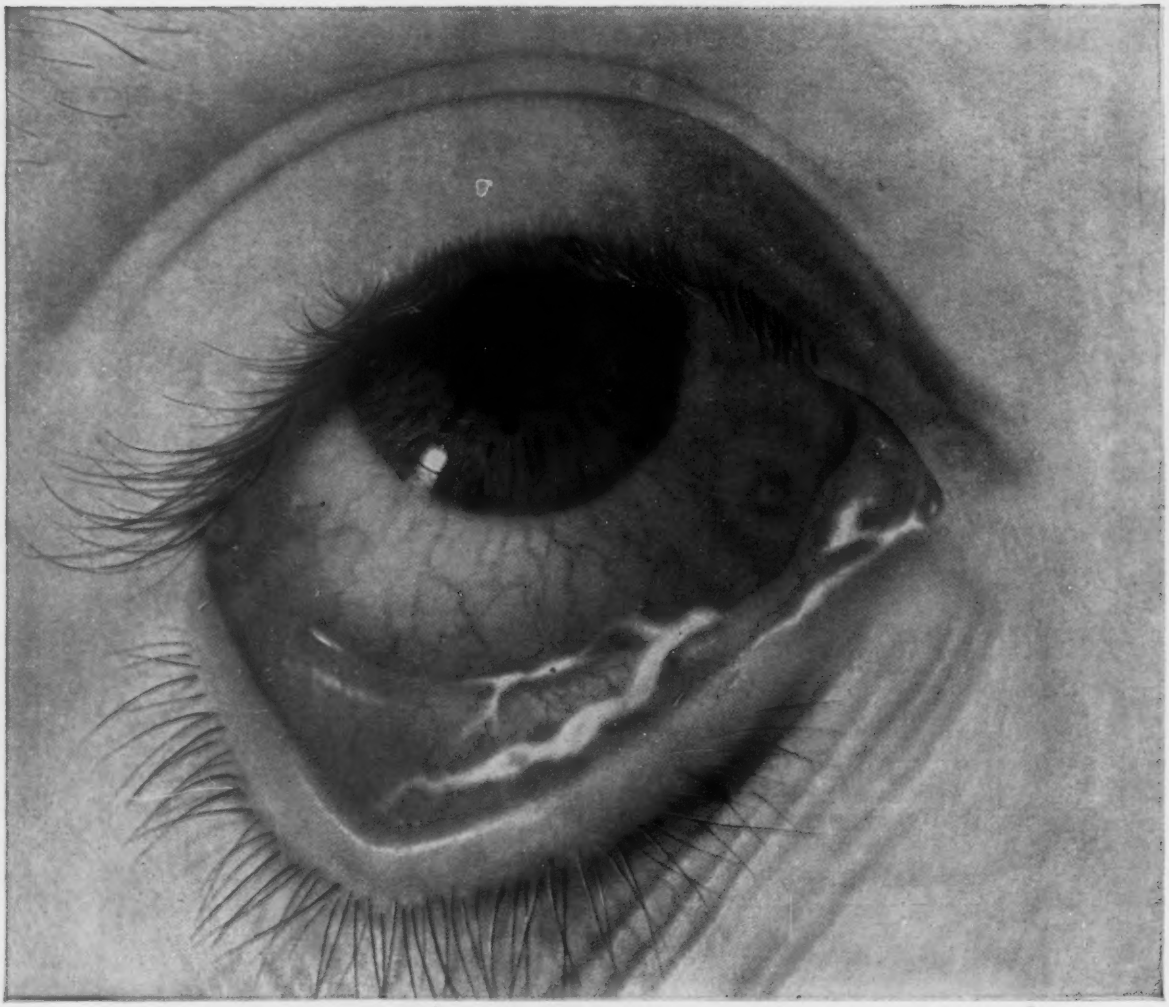

no irritating crystals[1] · uniform concentration in each drop[2]

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1. Lippmann, O.: Arch. Ophth. **57**:339, March 1957.
2. Gordon, D.M.: Am. J. Ophth. **46**:740, November 1958.

supplied: 0.5% Sterile Ophthalmic Solution NEO-HYDELTRASOL (with neomycin sulfate) and 0.5% Sterile Ophthalmic Solution HYDELTRASOL®. In 5 cc. and 2.5 cc. dropper vials. Also available as 0.25% Ophthalmic Ointment NEO-HYDELTRASOL (with neomycin sulfate) and 0.25% Ophthalmic Ointment HYDELTRASOL. In 3.5 Gm. tubes.

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MSD MERCK SHARP & DOHME Division of Merck & Co., Inc., Philadelphia 1, Pa.

Q

Shouldn't **KANTREX**® Injection* be kept in reserve for treating staph or gram-negative infections until other antibiotics have been tried first?

a

No. Naturally, KANTREX Injection should not be used in mild or self-limited infections, but as Yow states, "it should not be withheld in moderately severe or severe infections."[1]

Q *What properties of* KANTREX *led Yow to draw this conclusion?*

Next page, please . . .

*Kanamycin sulfate injection (Bristol)

MORE QUESTIONS on the clinical use of KANTREX®

Q *What properties of* KANTREX *led Yow to draw this conclusion?*

a The following[2]: (1) KANTREX Injection is bactericidal, not merely bacteriostatic; (2) it is absorbed rapidly after intramuscular injection; (3) it has proved successful in many types of staph and gram-negative infections resistant to other antibiotics; and (4) it is well tolerated when used judiciously.

Q *But if I use* KANTREX *Injection, won't that help make bacteria resistant to it?*

a Numerous investigators have reported that micro-organisms do not readily develop resistance to KANTREX in a clinical setting; and emergence of resistance to KANTREX has not been a practical problem.[3,4,5,6,7,8]

Q *How does the* in vitro *activity of* KANTREX *against staph compare with that of other antibiotics?*

a Griffith and Ostrander[9] tested 794 strains of staphylococci and found that 95.2% were sensitive to KANTREX. By contrast, only 15.5% of the same organisms were sensitive to penicillin, 33.5% to tetracycline, 52.4% to erythromycin, and 71.7% to chloramphenicol.

Q *What about the sensitivity of other pathogens to* KANTREX*?*

a Leming[10] recently summarized the *in vitro* activity of KANTREX against 4493 strains of various organisms isolated from hospital patients over a 7-month period. He reported that the following percentages of these clinical isolates were sensitive to KANTREX: *Proteus mirabilis*, 98%; *Proteus morganii*, 94%; *Proteus rettgeri*, 89%; *Proteus vulgaris*, 87%; *Paracolobactrum intermedium*, 96%; *Coli-aerogenes* group, 93%; *Streptococcus viridans*, 78%; *Salmonella* and *Shigella*, 92%.

Q *What do these figures mean clinically?*

a A great deal. As Yow stated in recent reviews of KANTREX Injection, it "appears to be one of the

most effective anti-staphylococcal antibiotics available today."[1,2] KANTREX Injection is also effective in the treatment of infections caused by "most strains of *E. coli, Proteus sp.*, the *Klebsiella pneumoniae-Aerobacter aerogenes* group, and many strains of *Pseudomonas aeruginosa* resistant to other antibiotics."[2] In another report, KANTREX Injection was placed at the head of the list of drugs "with the most chance of success" against *A. aerogenes* urinary tract infections.[11]

Q *Have these findings about* KANTREX *therapy been substantiated by other investigators?*

a Yes, indeed. Finegold,[12] who reviewed the clinical findings of 64 investigators, reported that infections which "usually responded" to KANTREX included: staph infections (including staph enteritis), *E. coli* infections (including *E. coli* gastroenteritis), atypical acid-fast bacillus infections, *Aerobacter-Klebsiella* infections, paracolon infections, *Alcaligenes* infections, *Shigella* dysentery, *Salmonella* enteritis, anthrax, amebiasis, and *E. histolytica* carrier state. Among the infections that "sometimes responded" were listed: pneumococcal infections, group A *beta*-hemolytic streptococcic infections, *Proteus* infections, gonorrhea, and paratyphoid fever.

Q *That's an impressive list. What didn't respond?*

a According to Finegold's tabulation, treatment failures were "usually" encountered in brucellosis, *Pseudomonas* infections, typhoid fever, mycotic infections and anaerobic infections.[12]

Q *How long do I have to give* KANTREX *Injection before I know whether it works or not?*

a Generally 2 or 3 days or less. Usually the effectiveness of KANTREX Injection can be determined in 24 to 36 hours. Rutenburg et al. reported that "the rapidity with which bacteria are killed by this agent is reflected by the promptness of the clinical response."[13]

Q *How long should I continue to administer* KANTREX?

a If definite clinical response does not occur within 5 days, KANTREX therapy should be stopped and the antibiotic sensitivity of the invading organism rechecked.

Q *What is the hazard of a patient developing hearing loss during* KANTREX *therapy?*

a In well hydrated patients with normal kidney function receiving KANTREX at the recommended dosage schedule, the hazard of ototoxic reactions is negligible. In patients with impaired kidney function, the risk of ototoxic reactions is sharply increased, and in such cases the dosage should be reduced. Finegold has stated: "Toxicity inherent in the drug can be avoided or minimized with careful management."[12]

Q *Why should renal impairment influence the dosage?*

a Because renal impairment delays the excretion of KANTREX Injection and causes an excessive accumulation in blood and tissues. Such excessive concentrations increase the risk of ototoxicity. Dosage recommendations emphasize that adequate serum levels can be achieved in such patients with a fraction of the dose suggested for patients with normal kidney function.

Q *Have you had any reports of blood dyscrasias?*

a None whatever.

Q *You mean, then, that a physician who uses* KANTREX *Injection judiciously should find it not only effective but also well tolerated?*

a Effective? Certainly, against almost all staph or "gram-negatives," even though they may be resistant to other antibiotics. Well tolerated? Yes, when given in recommended dosage. The physician can well agree with Yow, that while KANTREX Injection should not be used in mild or self-limited infections, "it should not be withheld in moderately severe or severe infections."[1] That, indeed, is the time to give it—first!

KANTREX® CAPSULES

for local gastrointestinal therapy...
not for systemic infections

Q *If* KANTREX *is not absorbed from the G.I. tract, what are the capsules used for?*

a Preoperative bowel sterilization, and local treatment of intestinal infections due to kanamycin-sensitive organisms.

Q *What types of intestinal infections, for instance?*

a Acute and chronic shigellosis,[14] acute and chronic salmonellosis,[4,14,15,16] amebiasis,[17] bacillary dysentery,[18] infantile diarrhea,[16,18] gastroenteritis,[19] and staphylococcal enterocolitis.[2]

Q *For preoperative bowel sterilization, why should I switch from neomycin to* KANTREX *Capsules?*

a Because KANTREX has been rated superior to neomycin for this purpose.[20,21,22] Out of 30 intestinal antiseptics studied, KANTREX was designated "the only single agent classified as a preferred drug."[21] KANTREX "consistently eliminated all aerobic bacteria within 72 hours (and often within 24 to 36 hours) if a purgative was given with the first dose to expedite passage through the gastrointestinal tract."[12]

Q *Is that all the advantage* KANTREX *has over neomycin for preoperative bowel sterilization?*

a Not at all, there are several others. Diarrhea, nausea and vomiting have not been observed with KANTREX, though they occur frequently with neomycin; yeasts do not proliferate, in contrast to rapid growth with neomycin; and clostridia are well controlled with KANTREX, and not controlled with neomycin.[20,21,22]

KANTREX®

INJECTION KANAMYCIN SULFATE INJECTION

INDICATIONS

Infections due to kanamycin-sensitive organisms, particularly staph or "gram-negatives": genito-urinary infections; skin, soft tissue and post-surgical infections; respiratory tract infections; septicemia and bacteremia; osteomyelitis and periostitis; staph enteritis and gastroenteritis.

DOSAGE: INTRAMUSCULAR ROUTE

Usual daily dose is 15 mg. per kg. of body weight, in 2 to 4 divided doses. (See detailed recommendations in insert accompanying each package.)

TOXICITY

When dosage recommendations are followed, the incidence of toxic reactions to KANTREX is low. In well hydrated patients under 45 years of age with normal kidney function, receiving a total dose of 20 Gm. or less of KANTREX, the risk of severe ototoxic reactions is negligible.

In patients with impaired renal function or pre-renal azotemia, the daily dose of KANTREX should be reduced to avoid accumulation of the drug in serum and tissues, thus minimizing the possibility of ototoxicity. In such patients, if therapy is expected to last 5 days or more, audiograms should be obtained prior to and during treatment. KANTREX therapy should be stopped if tinnitus or subjective hearing loss develops, or if audiograms show significant loss of high frequency response.

OTHER ROUTES OF ADMINISTRATION

KANTREX should be used by intravenous infusion only when the intramuscular route is impracticable. KANTREX can also be employed for intraperitoneal use, aerosol treatment, and as an irrigating solution. See package insert for directions.

PRECAUTIONS

Use of antibiotics may occasionally result in overgrowth of non-sensitive organisms. If superinfection appears during therapy, appropriate measures should be taken.

SUPPLY

Available in rubber-capped vials as a ready-to-use sterile aqueous solution in two concentrations (stable at room temperature indefinitely):

KANTREX Injection, 0.5 Gm. kanamycin (as sulfate) in 2 ml. volume.
KANTREX Injection, 1.0 Gm. kanamycin (as sulfate) in 3 ml. volume.

CAPSULES (for local gastrointestinal therapy; not for systemic medication)

INDICATIONS AND DOSAGE

For preoperative bowel sterilization: 1.0 Gm. (2 capsules) every hour for 4 hours, followed by 1.0 Gm. (2 capsules) every 6 hours for 36 to 72 hours.

For intestinal infections: Adults: 3.0 to 4.0 Gm. (6 to 8 capsules) per day in divided doses for 5 to 7 days. Infants and children: 50 mg. per kg. per day in 4 to 6 divided doses for 5 to 7 days.

PRECAUTION

Preoperative use of KANTREX Capsules is contraindicated in the presence of intestinal obstruction. Although only negligible amounts of KANTREX are absorbed through intact intestinal mucosa, the possibility of increased absorption from ulcerated or denuded areas should be considered.

SUPPLY

KANTREX Capsules, 0.5 Gm. kanamycin (as sulfate), bottles of 20 and 100.

REFERENCES:

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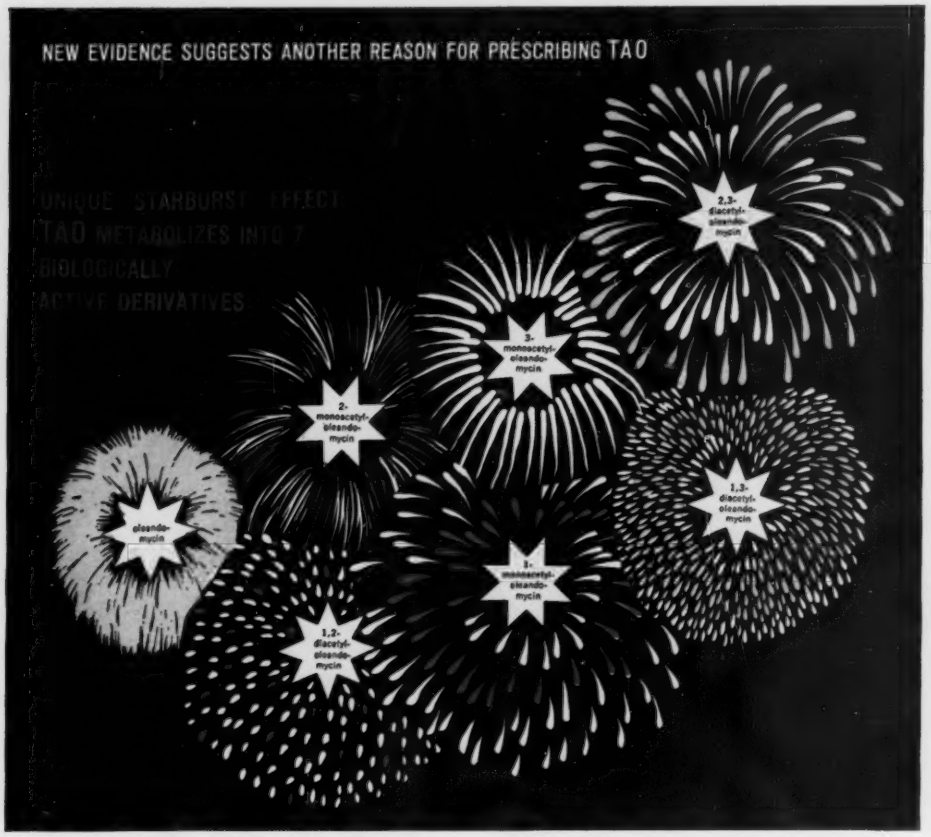

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1. English, A. R., and McBride, T. J.: Proc. Soc. Exper. Biol. & Med. 100:880 (Apr.) 1959. 2. Celmer, W. D.: Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959, p. 277. 3. English, A. R., and Fink, F. C.: Antibiotics & Chemother. 8:420 (Aug.) 1958.

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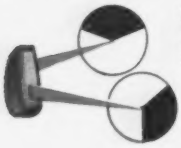

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1. Fabricant, N. D.: E.E.N.T. Monthly *37*:460 (July) 1958.
2. Lhotka, F. M.: Illinois M. J.: *112*:259 (Dec.) 1957.
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1. Spoor, H. J.: N. Y. State J. Med. Oct. 15, 1958

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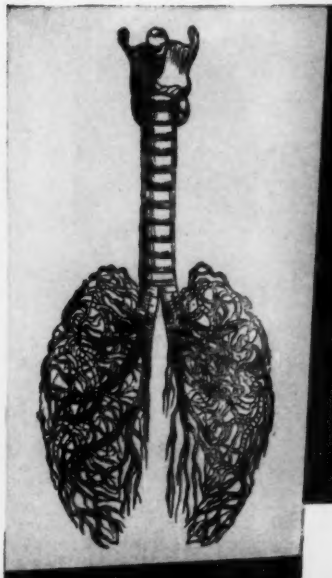

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Sulfamethazine	0.083 Gm.	0.166 Gm.
Pyrilamine Maleate	3.125 mg.	6.25 mg.
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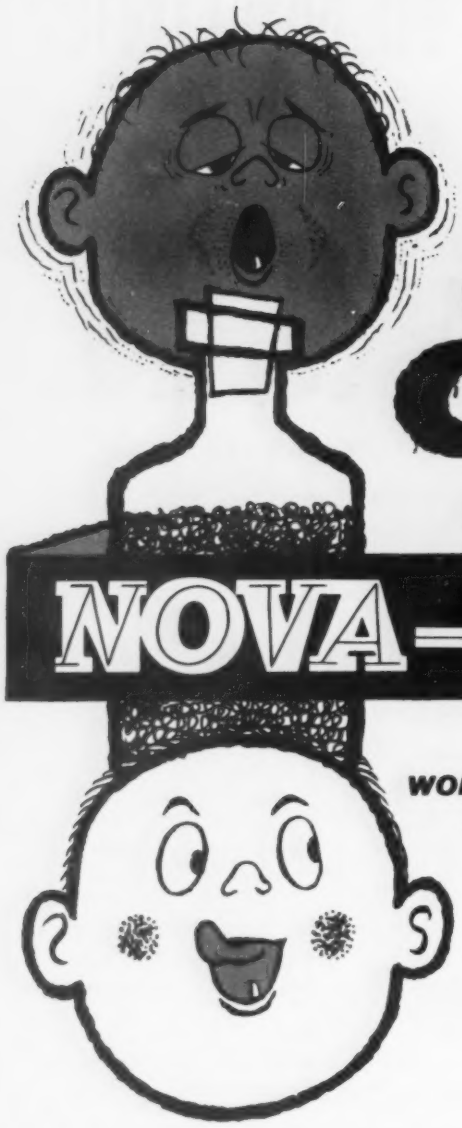

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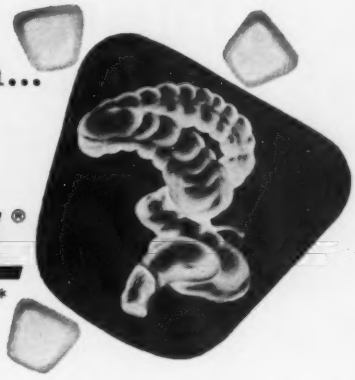

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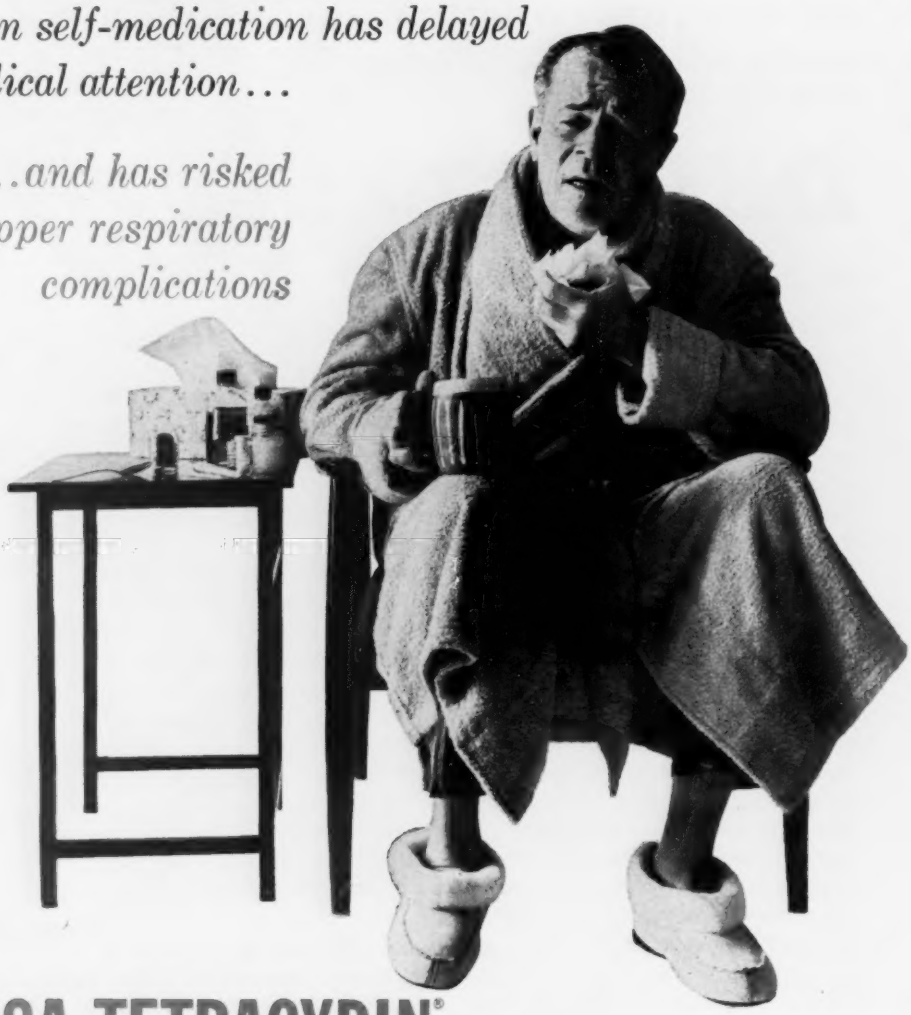

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each capsule contains:

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1. Kuzell, W. C., and others.: Arch. Int. Med. 92:646, 1953. 2. Wolfson, W. Q.: J. Michigan M. Soc. 54:323, 1955. 3. Strandberg, B.: Brit. J. Phys. Med. 19:9, 1956. 4. Platt, W. D., Jr., and Steinberg, I. H.: New England J. Med. 256:823 (May 2) 1957.

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in the Therapy of PNEUMONIA

Preferably, antibiotic therapy should be based on pretreatment culture of the offending pathogen, but in bacterial pneumonia the problem may well be too pressing to permit the required delay of 24 to 48 hours. A differential diagnosis among bacterial pneumonias, based on such clinical grounds as speed of onset, sepsis and pain may guide the choice of antibiotic for initiation of therapy.

Should clinical judgment dictate that antibiotic therapy be started immediately, at the same time a sputum sample or a subglottic swab can be sent to the laboratory for culture and sensitivity studies. If the response to the first antimicrobial agent proves unsatisfactory, a reasonable basis for changing therapy will then be at hand.

Choosing the Antibiotic

Since therapy must be started at once for bacterial pneumonia, it is advisable to choose a broad-spectrum antibiotic that quickly produces high levels of active agent (e.g., tetracycline phosphate complex, TETREX). Such an antibiotic probably has the best chance of controlling the pathogen, whether it be gram-negative or gram-positive. And if the laboratory report shows that the invading organism is much less sensitive to tetracycline than to other agents, the patient can then be changed to an appropriate antibiotic. If the difference in sensitivity is slight, then the possibility of side effects, sensitization, and toxicity should be evaluated before changing therapy to another antibiotic.

The greatest number of bacterial pneumonias are caused by pneumococci, which respond very well to penicillin, tetracycline, and chloramphenicol. Also, these antibiotics are usually effective against the other gram-positive coccal pneumonias. But penicillin is ineffective against the viral pneumonias and the gram-negative *Hemophilus influenzae* and *Klebsiella pneumoniae*. Although *K. pneumoniae* causes only about 1 to 2 per cent of pneumonia cases on the average,[1] these are apt to be acute and fulminating (Friedländer's pneumonia), with a high mortality rate if not effectively treated. Since pneumococcal pneumonia may be difficult to distinguish clinically from Friedländer's, except by gram-stained sputum smear, it may be wiser to start treatment with an agent also effective against Klebsiella.

Penicillin, however, in addition to having a limited spectrum, also causes many minor and some serious sensitivity reactions. In a recent survey[2] it was found that penicillin produced severe skin reaction. But most important was the observation that anaphylactic shock, with a fatality rate of about 9 per cent, was the most frequent serious reaction. Such severe reactions are almost always associated with parenteral administration.

Tetracycline is also clinically effective in primary atypical pneumonia.[3]

The tetracyclines (e.g., TETREX) have the advantage of a broad range of antimicrobial activity and low toxicity. And in addition, the physician does not have to trouble himself or his patients with repeated blood studies when he prescribes TETREX. Minor reactions such as gastric upsets or mild skin rashes occur occasionally. The most serious side effects are staphylococcal and monilial overgrowth, but these are rare and can be adequately controlled.

No one would deny that appropriate antibiotic therapy has greatly reduced morbidity and saved many lives of patients with bacterial pneumonia. Nevertheless, general supportive measures in the care of patients remain important even today. Especially in the desperately ill patient, antibiotics are not considered as substitutes for the individual evaluation, clinical observation and judgment of the physician.

Some Micro-organisms Susceptible[a] to Tetracycline (TETREX)[b]

Streptococcus; Staphylococcus; Pneumococcus; Gonococcus; Meningococcus; *C. diphtheriae; B. anthracis; E. coli;* Proteus; *A. aerogenes; Ps. aeruginosa; K. pneumoniae;* Shigella; Brucella; *P. tularensis; H. influenzae; T. pallidum;* Rickettsiae; Viruses of psittacosis and ornithosis, lymphogranuloma inguinale, primary atypical pneumonia; *E. histolytica; D. granulomatosis.*

a Some strains are not susceptible.

b Table adapted from Goodman, L. S., and Gilman, A.: The Pharmaceutical Basis of Therapeutics. 2nd edition, New York, The Macmillan Co., 1956, pp. 1322-1323.

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1. Ford, R. A., and Blanchard, K.: Journal-Lancet 78:185, 1958.

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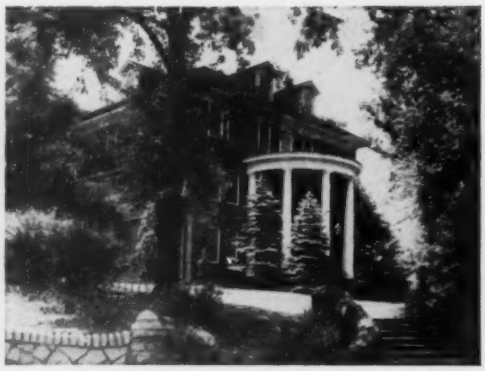

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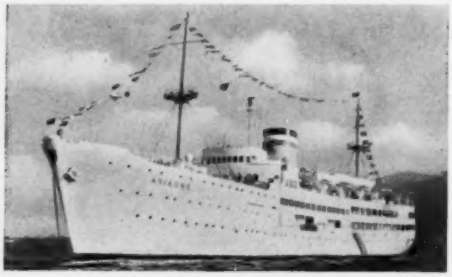

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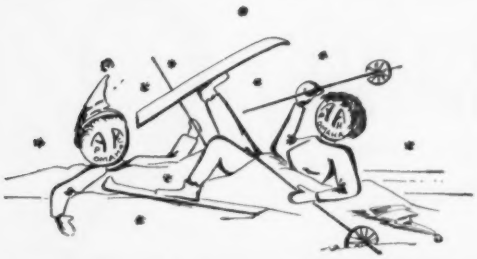

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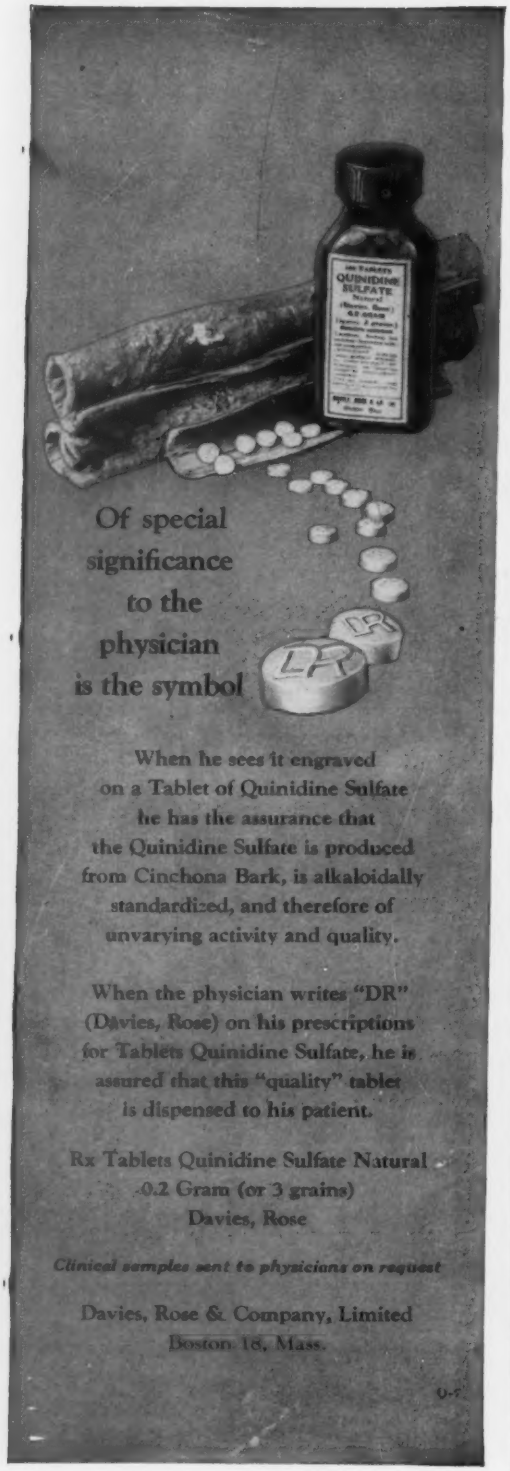
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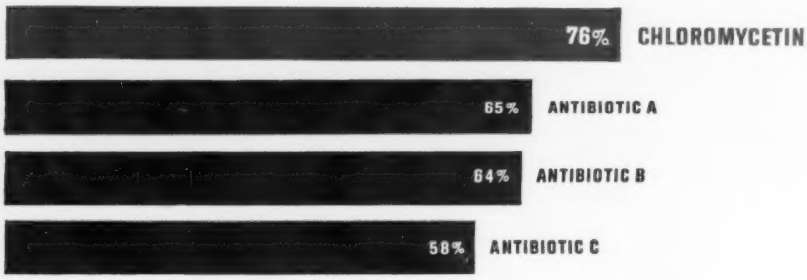

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